

# Strength training and risk of type 2 diabetes in a Japanese working population: A cohort study

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## Keywords

Cohort studies, Prevention, Resistance training

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## ABSTRACT

**Aims/Introduction:** Muscle strength training has been suggested to improve glucose metabolism; however, epidemiological evidence regarding strength training's effects on diabetes risk is scarce. We prospectively examined the association between strength training and the risk of type 2 diabetes in Japanese men and women.

**Materials and Methods:** The sample included health checkups on 26,630 Japanese male and female workers aged 30–64 years without diabetes at baseline. Weekly time spent on strength training was elicited using a self-reported questionnaire. Type 2 diabetes was diagnosed based on hemoglobin A1c, fasting glucose, random plasma glucose and self-report in an annual health checkup. Hazard ratio (HR) and its 95% confidence interval (CI) for incident diabetes was estimated using a Cox proportional hazards model.

**Results:** During a mean follow up of 5.2 years with 139,748 person-years, 1,770 individuals developed diabetes. Age- and sex-adjusted HR for diabetes was 0.58 (95% CI 0.42–0.79) in those who engaged in strength training compared with those who engaged in no strength training. After further adjusting for potential confounders, the corresponding HR was 0.66 (95% CI 0.48–0.90). Additional adjustment for body mass index did not materially change the result; the HR was 0.70 (95% CI 0.51–0.96). The association was more pronounced in individuals aged 50 years or older than those aged <50 years, although the difference in the association by age was not significant.

**Conclusions:** These results suggest that engagement in strength training could help to reduce the risk of type 2 diabetes in a Japanese working population.

## INTRODUCTION

Diabetes is a major risk factor for vascular disease<sup>1,2</sup>, and accounted for 1.3 million deaths in 2008<sup>3</sup>. Recent statistics show that diabetes affects 382 million adults worldwide<sup>4</sup>, and this number is estimated to rise to 592 million by 2035<sup>4</sup>. Physical activity plays an important role in the prevention of type 2 diabetes. Accumulated evidence suggests that moderate- to vigorous-intensity physical activity<sup>5</sup> or aerobic exercise including walking<sup>5</sup> and running<sup>6</sup> can prevent the development of type 2 diabetes. However, less attention has been paid to the role of other forms of physical activity in the pathogenesis of this metabolic disease.

Muscle strength training is a form of physical activity specifically designed to increase muscular power and endurance<sup>7</sup>. This type of training has been shown to improve insulin sensitivity<sup>8</sup>, an important determinant of type 2 diabetes. Recent meta-analyses of randomized controlled trials among patients with type 2 diabetes reported that strength training<sup>9</sup> or strength training combined with aerobic exercise<sup>10</sup> improved glycemic control. Therefore, it is anticipated that strength training prevents the development of type 2 diabetes.

Epidemiological evidence on this issue is, however, scarce and limited to a Western population. Two US cohort studies<sup>11,12</sup> showed that the number of hours spent weekly on muscle strengthening activities was inversely associated with the risk of type 2 diabetes, which was determined based on

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self-report. Given that Asians have less muscle mass<sup>13–15</sup> and lower insulin secretory capacity<sup>15</sup> than Caucasians, additional research on this topic is required in Asian populations. In the present study, we prospectively investigated the association between strength training and the risk of type 2 diabetes in Japanese men and women; the presence of type 2 diabetes was assessed using fasting glucose and hemoglobin A1c (HbA1c), a diagnostic test for diabetes, which was recently adopted by the International Expert Committee<sup>16</sup>.

## MATERIALS AND METHODS

### Setting and Participants

The present study was part of the Japan Epidemiology Collaboration on Occupational Health Study, an ongoing, multicenter epidemiological study involving workers from several companies in Japan. In one of the participating companies, detailed information on physical activity has been collected at periodic health checkups since 2006. The present prospective analysis was based on data of annual health checkups in 2006 (baseline) and from 2007 through 2013 (a maximum of 6 years of follow up). Before the collection of data, the conduct of the Japan Epidemiology Collaboration on Occupational Health Study was announced in each company through posters that explained its purpose and procedure. Participants did not provide their verbal or written informed consent to join the study, but were given the opportunity to refuse to participate. This procedure conforms with the Japanese Ethical Guidelines for Epidemiological Research, which state that informed consent is not necessarily required for observational studies using existing data. The study protocol was approved by the ethics committee of the National Center for Global Health and Medicine, Japan.

Participants were workers at a large participating company where detailed information on leisure-time physical activity was obtained at health checkups. A total of 42,329 workers (35,378 men and 6,951 women) aged 30–64 years underwent health examinations between April 2006 and March 2007 (baseline). Of these, we excluded 11,434 workers; 3,376 were patients with diabetes, 7,665 were missing information on variables required to diagnose diabetes at baseline and 766 reported having a history of cancer, cardiovascular disease or stroke. We further excluded 2,961 subjects; 2,515 were missing information on exposure or covariates and 487 only engaged in unspecified leisure-time physical activity (named ‘other’). Some participants met more than one exclusion criterion. Finally, we excluded 1,304 subjects who did not attend any subsequent health checkup or who attended, but did not receive, HbA1c or blood glucose measurement in any subsequent health examination. In total, 26,630 workers (23,207 men and 3,423 women) aged 30–64 years remained for analysis.

### General Health Examination

Lifestyle factors including physical activity, smoking, alcohol use, sleep duration, personal and family history of disease, and work-related conditions were ascertained through a standard

questionnaire at the time of health checkup. Total alcohol consumption was calculated using information on frequency (number of days per week) and amount of alcohol consumption of common beverages (Japanese sake, beer, whiskey, shochu, chuhai and wine) per day, which was indicated by an equivalent volume of one unit (go) of Japanese sake. One go of Japanese sake contains approximately 23 g of ethanol. Body height was measured to the nearest 0.1 cm and bodyweight to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m<sup>2</sup>). Systolic and diastolic blood pressures were measured using an oscillometric method with an automated sphygmomanometer (BP-203RV III; Colin, Tokyo, Japan) in a sitting position after 3 min of rest. Blood glucose levels were determined using the glucose electrode technique with an ADAMS glucose GA-1170 device (Arkray, Kyoto, Japan). HbA1c was measured by high-performance liquid chromatography with an ADAMS-HA8160 device (Arkray), and it was converted to the National Glycohemoglobin Standardization Program equivalent value (%) using the formula<sup>17</sup>:

$$\text{HbA1c (\%)} = 1.02 \times \text{HbA1c (Japan Diabetes Society) (\%)} + 0.25\%.$$

### Assessment of Physical Activity

Participants were asked if they regularly engaged in any physical activity during leisure time; if they did engage, they were further asked to choose up to three activities from a list of 20, including muscle strength training, and report the frequency (times per month) and duration of exercise per occasion (measured in minutes) for each activity. If participants engaged in activities that were not listed in the questionnaire, they were instructed to choose an activity of similar intensity from the list.

Based on the strength training data, participants were classified into two groups; those who engaged in strength training and those who did not. Of the remaining 19 regular exercise or sports activities, one activity named ‘other’ was not used for further analysis. The metabolic equivalent (MET) value for each activity was assigned according to a compendium of physical activities<sup>18</sup>. If the MET value of an activity was not listed in the compendium, we assigned a MET value of a similar activity. Therefore, 18 activities with three or more METs were used to calculate weekly MET-hours of aerobic exercise by multiplying the METs, duration and frequency of the activity; aerobic exercise was categorized into four categories: none and tertiles of the rest (low, moderate and high).

### Ascertainment of Type 2 Diabetes Cases

Type 2 diabetes was defined by HbA1c  $\geq 6.5\%$  (48 mmol/mol), fasting glucose  $\geq 126$  mg/dL (7.0 mmol/L), random plasma glucose  $\geq 200$  mg/dL (11.1 mmol/L), history of diabetes or current medication for diabetes based on the recent criteria by American Diabetes Association<sup>19</sup>. Individuals without diabetes at baseline

who met any of these conditions in the subsequent health checkups were considered to have incident type 2 diabetes.

### Statistical Analysis

Means (standard deviations) and percentages of study variables were calculated for the two strength training groups. Person-time was calculated from the date of the baseline examination to the first date when diabetes was confirmed at a follow-up examination or to the date of the most recent examination, whichever came first. Hazard ratio (HR) and its 95% confidence interval (CI) for the incidence of diabetes with respect to strength training were calculated using Cox proportional-hazards regression models. We established the age- and sex-adjusted model, and the following multivariable-adjusted models. Multivariate model 1 was adjusted for age (year, continuous), sex, shift work (yes or no), occupational physical activity (mostly sitting, mostly standing, walking often or fairly active), smoking status (non-smoker, current smoker consuming 1–10, 11–20 or  $\geq 21$  cigarettes per day), alcohol consumption (non-drinker, drinker consuming  $< 1$ , 1 to  $< 2$  or  $\geq 2$  go of Japanese sake equivalent per day, 1 go of Japanese sake contains approximately 23 g of ethanol), sleep duration ( $< 5$ , 5 to  $< 6$ , 6 to  $< 7$  or  $\geq 7$  h per day), aerobic exercise (none, low, moderate or high), hypertension (defined as systolic blood pressure  $\geq 140$  mmHg, diastolic blood pressure  $\geq 90$  mmHg or current medication for hypertension [yes or no]) and family history of diabetes (yes or no). BMI ( $< 18.5$ , 18.5 to  $< 23$ , 23 to  $< 25$ , 25 to  $< 30$  or  $\geq 30$  kg/m<sup>2</sup>) was additionally adjusted for in model 2. We carried out stratified analyses by age ( $< 50$  and  $\geq 50$  years), sex, BMI ( $< 25$  and  $\geq 25$  kg/m<sup>2</sup>), occupational physical activity (sedentary and not sedentary), smoking (non-smoker and current smoker), aerobic exercise (none to low and moderate to high) and family history of diabetes (yes and no) to explore potential effect modifications. We tested the effect modification using a likelihood ratio test by comparing models with and without interaction terms. We tested the proportional-hazards assumption with the Schoenfeld residuals. We found no significant deviations for any covariate except smoking. We carried out a sensitivity analysis excluding those who were under medication for hypertension or dyslipidemia, because use of antihypertensive drugs<sup>20,21</sup> and cholesterol-lowering drugs<sup>22,23</sup> could influence insulin sensitivity and the risk of diabetes. Two-sided *P*-values  $< 0.05$  were considered statistically significant. All analyses were carried out with Stata version 13.1 (Stata Corp., College Station, TX, USA).

### RESULTS

Of the 26,630 participants (mean age 45.3 years), 1,770 developed type 2 diabetes during a mean follow-up time of 5.2 years with 139,748 person-years. At baseline, 1,090 (4.1%) engaged in strength training; 408 engaged in  $\geq 60$  min of strength training per week. Baseline characteristics by strength training status are shown in Table 1. Participants engaging in strength training

were younger and more likely to be male, to be non-smokers, and to engage in sedentary work and more aerobic exercise; they had a lower prevalence of obesity and hypertension than those not engaging in strength training. Other variables including shift work, alcohol use, sleep duration and family history of diabetes were not appreciably different between the categories of strength training.

The association between strength training and the risk of type 2 diabetes is shown in Table 2. Age- and sex-adjusted model showed that the adjusted HR for developing diabetes in participants who engaged in strength training was 0.58 (95% CI 0.42–0.79) as compared with those who did not engage in. Additional adjustment for smoking, alcohol consumption, sleep duration, aerobic exercise, occupational physical activity, shift work, hypertension and family history of diabetes attenuated the result; the corresponding HR in those who engaged in strength training was 0.66 (95% CI 0.48–0.90) in multivariable-adjusted model 1. Further adjustment for BMI did not materially change the inverse association; the HR (95% CI) was 0.70 (95% CI 0.51–0.96). After exclusion of 2,812 patients who were taking medication for hypertension or dyslipidemia, the results were not materially changed; those who engaged in strength training had a HR of 0.66 (95% CI 0.47–0.94) in multivariable-adjusted model 1 and 0.70 (95% CI 0.49–0.99) after further adjustment for BMI. As shown in Table 3, stratified analysis showed a stronger association between strength training and a lower risk of type 2 diabetes in individuals aged 50 years or older than in those aged  $< 50$  years, although this difference did not reach statistical significance (*P* for interaction = 0.21).

**Table 1** | Baseline characteristics by level of strength training

	Strength training	
	No	Yes
Participants (n)	25,540	1,090
Mean age, years (SD)	45.3 (8.4)	43.6 (8.2)
Men (%)	87.0	89.6
Mean BMI, kg/m <sup>2</sup> (SD)	23.4 (3.2)	23.2 (2.7)
BMI $\geq 25$ kg/m <sup>2</sup> (%)	27.5	22.3
Shift work (%)	18.8	19.2
Occupational physical activity – sedentary (%)	59.6	64.4
Mean leisure time aerobic exercise MET-hours per week (SD)	3.8 (10.4)	10.5 (15.0)
Current smoker (%)	42.9	28.7
Current drinker (%)†	29.0	29.0
Sleeping $< 6$ h per day (%)	50.7	50.6
Hypertension (%)	17.8	13.1
Family history of diabetes (%)	13.9	13.7

†Consuming  $\geq 1$  go of Japanese sake equivalent per day, 1 go of Japanese sake contains approximately 23 g of ethanol. BMI, body mass index; MET, metabolic equivalent; SD, standard deviation.

**Table 2** | Hazard ratios with 95% intervals for type 2 diabetes by level of strength training

	Strength training	
	No	Yes
Person-years	133,903	5,845
No. cases	1,729	41
Cases per 10,000 person-years	129	70
Age- and sex-adjusted model	1.00 (reference)	0.58 (0.42–0.79)
Multivariable-adjusted model 1†	1.00 (reference)	0.66 (0.48–0.90)
Multivariable-adjusted model 2‡	1.00 (reference)	0.70 (0.51–0.96)

†Adjusted for age (continuous), sex, smoking status (non-smoker or current smoker consuming 1–10, 11–20 or  $\geq 21$  cigarettes per day), alcohol consumption (non-drinker or drinker consuming  $<1$ , 1 to  $<2$  or  $\geq 2$  go of Japanese sake equivalent per day, 1 go of Japanese sake contains approximately 23 g of ethanol), sleep duration ( $<5$ , 5 to  $<6$ , 6 to  $<7$  or  $\geq 7$  h per day), aerobic exercise (none, low, moderate or high), hypertension (presence or absence), shift work (yes or no), occupational physical activity (mostly sitting, mostly standing, walking often or fairly active) and family history of diabetes (presence or absence). ‡Adjusted for factors in model 1 plus body mass index ( $<18.5$ , 18.5 to  $<23$ , 23 to  $<25$ , 25 to  $<30$  or  $\geq 30$  kg/m<sup>2</sup>).

## DISCUSSION

In the present study of Japanese workers, strength training was associated with a lower risk of developing type 2 diabetes. The inverse association among workers aged over 50 years was stronger than that among those aged  $<50$  years, although the difference in the association by age was not significant. This is the first study to examine the association of strength training with incident diabetes in an Asian population.

We observed that participants who engaged in muscle strength training had a 34% lower risk of developing diabetes than those who did not even after adjustment for the array of confounders including occupational physical activity and aerobic exercise. This finding agrees with two previous US studies; the Health Professionals Follow-up Study (HPFS)<sup>11</sup> and the Nurses' Health Study (NHS) I and II<sup>12</sup> reported that longer weekly duration of muscle strengthening activity was associated with a lower risk of type 2 diabetes. In these studies<sup>11,12</sup>, however, diabetes was assessed by self-reported diagnosis, although a supplementary questionnaire was administered to confirm the diagnosis by obtaining information on symptoms, treatment and diagnostic test results<sup>11,12</sup>. We identified the incidence of type 2 diabetes using several methods including blood glucose, HbA1c and self-report. The present results extend the previous findings of predominantly Caucasian populations<sup>11,12</sup> to an Asian population.

The present finding is also in agreement with previous findings from studies using different designs. Cross-sectional

studies<sup>24,25</sup> have shown that muscle-strengthening activity and muscle mass were associated with higher insulin sensitivity. Strength training has been shown to improve insulin sensitivity in healthy men<sup>26</sup> and women<sup>27</sup>, and to increase the level of glucose transporter type 4, which is responsible for glucose uptake, in young men<sup>28</sup> and patients with diabetes<sup>29</sup>. For patients with type 2 diabetes, the American College of Sports Medicine and the American Diabetes Association<sup>30</sup> recommends 150 min per week of aerobic exercise and 2–3 days per week of resistance training. A recent meta-analysis of randomized controlled trials among patients with type 2 diabetes<sup>31</sup> showed that weekly volume of strength training combined with aerobic exercise was associated with improved glycemic status in a dose–response manner. The present results together with accumulating evidence support the beneficial role of strength training in the prevention as well as the control of type 2 diabetes.

We observed a stronger association between strength training and a lower risk of type 2 diabetes among workers aged 50 years or older than among their counterparts, although the difference by age was not statistically significant. The present results differ from those of previous studies; the NHS reported no significant difference in the association of muscle-strengthening activities with risk of type 2 diabetes between women aged  $<65$  and  $\geq 65$  years<sup>12</sup>, whereas the HPFS showed that strength training was associated with a lower risk of type 2 diabetes in men aged  $<65$  years, but not in those aged  $\geq 65$  years<sup>11</sup>. We do not have clear explanations for these discordant results. Such discrepancies in effect modification by age among studies might be ascribed to methodological differences including age category cut-offs, participant characteristics (i.e., sex and ethnicity), assessment of muscle strengthening activities and diagnosis of diabetes.

We did not observe a reduction in type 2 diabetes risk associated with strength training in women (HR 0.99), although the interaction by sex was not statistically significant. Given a small number of women who engaged in strength training in the present study ( $n = 113$ ), random variation might be a plausible explanation for the null finding in women. Alternatively, this result could reflect lower intensity of strength training in women than in men and less muscular adaptation to strength training in women than in men<sup>32,33</sup>. Nevertheless, the NHS<sup>12</sup> showed a significant inverse association between muscle-strengthening activities and risk of type 2 diabetes in women, supporting a protective role of strength training in women.

The mechanisms underlying the inverse association between strength training and the risk of type 2 diabetes are not fully elucidated, but some pathways are suggested. Strength training stimulates glycogen synthesis, which leads to reduced blood glucose levels by inhibiting glycogen synthase kinase  $\beta$  by AKT<sup>34</sup>. Strength training increases muscle mass and resting energy expenditure<sup>26</sup>, resulting in decreased fat mass<sup>26</sup>. Decreasing body fat increases levels of adiponectin<sup>35</sup>, an insulin sensitizer<sup>36</sup>, and decreases pro-inflammatory cytokines, reactive oxygen species and endoplasmic reticulum stress<sup>37</sup>, all of which can worsen insulin sensitivity<sup>37</sup>.

**Table 3** | Strength training and risk of type 2 diabetes according to potential risk factors for type 2 diabetes

	No. cases	Person-years	No strength training	Engaging in strength training	<i>P</i> for interaction†
			Adjusted HRT (95% CI)		
Age (years)					
≥50	807	41,043	1.00 (reference)	0.45 (0.25–0.83)	0.21
<50	963	98,705	1.00 (reference)	0.79 (0.55–1.15)	
Sex					
Male	1,654	122,730	1.00 (reference)	0.64 (0.46–0.89)	0.53
Female	116	17,018	1.00 (reference)	0.99 (0.30–3.24)	
BMI (kg/m <sup>2</sup> )					
≥25	891	37,422	1.00 (reference)	0.58 (0.36–0.95)	0.56
<25	879	102,326	1.00 (reference)	0.83 (0.54–1.25)	
Smoking					
Smoker	863	59,856	1.00 (reference)	0.67 (0.40–1.12)	0.70
Non-smoker	907	79,892	1.00 (reference)	0.67 (0.45–1.05)	
Aerobic exercise					
None or low	1,400	108,344	1.00 (reference)	0.64 (0.40, 1.04)	0.98
Moderate or high	370	31,404	1.00 (reference)	0.68 (0.45, 1.03)	
Occupational PA					
Sedentary	1,063	84,274	1.00 (reference)	0.73 (0.50, 0.94)	0.34
Non-sedentary	707	55,474	1.00 (reference)	0.51 (0.28, 0.99)	
Shift work					
Shift worker	317	26,943	1.00 (reference)	0.55 (0.24, 1.25)	0.58
Non-shift worker	1,453	112,805	1.00 (reference)	0.69 (0.49, 0.97)	
Family history of DM					
Presence	412	19,023	1.00 (reference)	0.55 (0.27, 1.12)	0.56
Absence	1,358	120,726	1.00 (reference)	0.70 (0.49, 0.99)	

†Adjusted for age, sex, smoking status (non-smoker or current smoker consuming 1–10, 11–20 or ≥21 cigarettes per day), alcohol consumption (non-drinker or drinker consuming <1, 1 to <2, or ≥2 go of Japanese sake equivalent per day, 1 go of Japanese sake contains approximately 23 g of ethanol), sleep duration (<5, 5 to <6, 6 to <7 or ≥7 h per day), aerobic exercise (none, low, moderate or high), hypertension (presence or absence), shift work (yes or no), occupational physical activity (mostly sitting, mostly standing, walking often or fairly active) and family history of diabetes (presence or absence). ‡Calculated using a likelihood ratio test comparing models with and without interaction terms between strength training and the potential risk factors for type 2 diabetes. BMI, body mass index; CI, confidence interval; DM, diabetes mellitus; HR, hazard ratio; PA, physical activity.

The strengths of the present study include a large population size and annual follow-up assessment of diabetes using both HbA1c and blood glucose. The present study also has several limitations. First, the physical activity questionnaire used in the present study was not validated. Additionally, the questionnaire was not designed to obtain detailed information on strength training (i.e., the type and intensity of strength training). Nevertheless, the HPFS<sup>11</sup>, in which only weekly hours of weight training (any type) was ascertained, showed an inverse association with risk of diabetes. Participants in the present study were allowed to choose up to three types of physical activities; thus participants might not report strength training if they engaged in three or more activities other than strength training. Second, as reported in a previous Japanese study<sup>38</sup>, the proportion of adults who engaged in strength training in the present study (i.e., <5%) was much lower than those in US studies (17.4% of men engaged in weightlifting in the HPFS<sup>11</sup>, and 41.7% of women engaged in resistance exercise or lower intensity muscle

conditioning exercise in the NHS<sup>12</sup>). Due to few cases of diabetes in the highest category of strength training, we did not assess the dose–response relationship. Third, we used only baseline information for physical activity assessment. Participants might have changed their physical activities including strength training during follow up. Nevertheless, these types of changes would lead to underestimation rather than overestimation. Fourth, participants who engaged in strength training appeared to be health conscious given that they engaged in more aerobic exercise and tended to be non-smokers (Table 1). Although we adjusted for these factors in analysis, we cannot exclude the possibility of overestimation as a result of potential confounding by unmeasured variables including sedentary time, which has been linked to diabetes risk independently of physical activity<sup>39</sup>. Finally, the participants were young and middle-aged workers in a large company. Therefore, caution must be taken in generalizing our findings to workers in small- to middle-sized companies, non-working populations or elderly populations.

In conclusion, the present study showed that engagement in muscle strength training is associated with a lower risk of type 2 diabetes in a Japanese population. The magnitude of the reduced risk associated with strength training in workers aged 50 years or more tended to be greater than the reduction in those aged <50 years. Further studies are required to clarify the type, frequency and duration of muscle strengthening activities that contribute to the prevention of type 2 diabetes.

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## DISCLOSURE

The authors declare no conflict of interest.

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