

# Letters

## RESEARCH LETTER

### HEALTH CARE REFORM

#### Effect of Moderate and Vigorous Aerobic Exercise on Incident Diabetes in Adults With Obesity: A 10-Year Follow-up of a Randomized Clinical Trial

Lifestyle intervention consisting of diet and regular exercise has proved to be effective for prevention of type 2 diabetes in individuals at high risk.<sup>1-3</sup> However, the isolated effect of vigorous and moderate exercise on prevention of diabetes is uncertain.



Supplemental content

In the current randomized clinical trial, we assessed the long-term effect of vigorous and moderate exercise on incident diabetes over a 10-year follow-up after a 12-month exercise intervention.

**Methods** | The study was approved by the Zhongshan Hospital of Fudan University institutional review board. All participants provided written informed consent. The [CONSORT](#) reporting guideline was followed.

We have conducted a 10-year follow-up study based on our previous randomized clinical trial to assess the long-term effects of exercise on the prevention of diabetes between July 2021 and May 2022 ([NCT05346250](#)) ([Supplement 1](#)). The randomized clinical trial of 12-month intervention consisted of vigorous aerobic exercise (n = 73), moderate aerobic exercise (n = 73), and nonexercise control groups (n = 74) in participants with central obesity and nonalcoholic fatty liver disease ([NCT01418027](#)) (eFigure in [Supplement 2](#)). Details of the intervention have been described previously.<sup>4</sup> At the end of 12-month active exercise intervention, all participants were

**Table 1. Trajectory of Fasting Plasma Glucose, Hemoglobin A<sub>1c</sub>, Body Weight, Waist Circumference, and Leisure Time Physical Activity Over 10-Year Follow-up**

				P value		
Variable	Nonexercise	Moderate exercise group	Vigorous exercise group	Moderate vs nonexercise	Vigorous vs nonexercise	Vigorous vs moderate exercise
Body weight, mean (SD), kg						
Baseline	72.1 (8.5)	71.1 (10.1)	71.7 (10.1)	.53	.81	.70
End of 1-y intervention	71.0 (8.5)	68.7 (10.3)	67.8 (10.0)	.15	.05	.56
At 2-y follow-up	71.5 (9.1)	69.5 (10.3)	69.1 (10.5)	.24	.17	.82
At 10-y follow-up	73.0 (8.4)	71.7 (10.6)	71.5 (10.0)	.47	.41	.93
Waist circumference, mean (SD), cm						
Baseline	96.1 (6.9)	95.7 (6.7)	95.2 (7.4)	.72	.44	.68
End of 1-y intervention	95.9 (7.0)	94.0 (6.8)	92.0 (7.4)	.11	.001	.11
At 2-y follow-up	97.3 (6.8)	96.1 (7.3)	94.4 (8.4)	.35	.03	.20
At 10-y follow-up	101.4 (7.9)	96.8 (6.8)	96.6 (8.3)	.001	<.001	.88
Fasting plasma glucose, mean (SD), mg/dL						
Baseline	103.5 (9.1)	104.0 (9.3)	102.6 (10.9)	.78	.56	.40
End of 1-y intervention	98.7 (8.9)	97.8 (9.4)	98.5 (11.0)	.61	.90	.71
At 2-y follow-up	100.5 (14.4)	97.9 (8.1)	100.9 (12.2)	.21	.86	.15
At 10-y follow-up	109.4 (18.5)	104.8 (17.3)	106.4 (19.2)	.17	.36	.63
Hemoglobin A <sub>1c</sub> , mean (SD), %						
Baseline	6.03 (0.31)	6.01 (0.33)	6.00 (0.36)	.64	.48	.80
End of 1-y intervention	6.05 (0.38)	5.94 (0.39)	5.94 (0.40)	.09	.09	.99
At 2-y follow-up	5.98 (0.39)	5.83 (0.37)	5.88 (0.45)	.05	.16	.55
At 10-y follow-up	6.25 (0.74)	5.95 (0.68)	5.96 (0.57)	.02	.02	.92
Leisure time physical activity, median (IQR), MET-h/w						
Baseline	11.6 (0-34.7)	11.6 (0-23.1)	13.3 (1.7-37.3)	.86	.40	.31
End of 1-y intervention	15.4 (5.5-32.4)	33.1 (15.0-44.7)	31.0 (17.7-44.7)	.04	.01	.68
At 2-y follow-up	14.6 (0-34.7)	23.1 (8.0-39.6)	21.0 (9.9-42.0)	.22	.21	.98
At 10-y follow-up	17.3 (6.6-23.1)	23.1 (4.0-34.7)	23.1 (13.0-46.2)	.09	.08	.98

Abbreviations: h/w, hours per week; MET, metabolic equivalents.

SI conversion factors: To convert fasting plasma glucose to mmol/L, multiply by

0.0555; hemoglobin A<sub>1c</sub> (glycated hemoglobin) to proportion of total hemoglobin, multiply by 0.01.

Table 2. Effects of Moderate Exercise and Vigorous Exercise vs Nonexercise Control Group on Risk of Incident Diabetes<sup>a</sup>

Characteristic	No. of cases	Incidence rate, per 100 PYs	Unadjusted model		Age, sex-adjusted model	
			RR (95% CI)	P value	RR (95% CI)	P value
2-y Follow-up						
Nonexercise group	8	5.4	1 [Reference]	NA	1 [Reference]	NA
Moderate exercise group	5	3.4	0.61 (0.20-1.85)	.36	0.58 (0.19-1.78)	.31
Vigorous exercise group	7	4.8	0.86 (0.31-2.38)	.76	0.83 (0.30-2.32)	.71
10-y Follow-up						
Nonexercise group	30	4.1	1 [Reference]	NA	1 [Reference]	NA
Moderate exercise group	14	1.9	0.47 (0.25-0.89)	.01	0.46 (0.25-0.87)	.01
Vigorous exercise group	15	2.1	0.51 (0.27-0.94)	.01	0.50 (0.27-0.93)	.01

Abbreviations: NA, not applicable; PY, person-year; RR, relative risk.

<sup>a</sup> Analyses were based on the intention-to-treat principle.

encouraged to continue with healthy lifestyle and moderate intensity aerobic exercise. Participants were followed up at 2-year and 10-year visits to assess the incidence of type 2 diabetes and the changes in body weight, waist circumference, and metabolic risk factors.<sup>5</sup> Baseline characteristics of participants lost in follow-up tended to be similar with participants who remained in follow-up (eTable in Supplement 2). Incident diabetes was defined as fasting plasma glucose of 126 mg/dL or greater, hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels of 6.5% or greater, and/or use of antidiabetic medication.

The Breslow-Cox regression model was used to estimate the relative risk (RR) for incident diabetes by intention-to-treat principle. Group differences were evaluated using the general linear model for continuous variables. Statistical significance was assessed at 2-sided  $P < .05$ .

**Results** | Of 220 eligible participants, 208 (94.5%) participants completed 1-year exercise intervention, 195 (88.6%) and 179 participants (81.4%; 32.3% male participants; mean [SD] age, 53.9 [7.1] years; waist circumference, 96.1 cm at baseline) remained for assessment of incident diabetes at 2-year and 10-year follow-up visits, respectively. The metabolic equivalents of leisure time physical activity were similar among the 3 groups at baseline and were higher in moderate and vigorous exercise groups than in the nonexercise group at the end of 1-year intervention. Although no significant differences were observed among the 3 groups at 10-year follow-up, there was a trend of higher levels of leisure time physical activity in the exercise groups than in the nonexercise group (Table 1).

Over the 10-year follow-up, the cumulative incidence of type 2 diabetes was 2.1 per 100 person-years (PYs), 1.9 per 100 PYs, and 4.1 per 100 PYs, respectively in the vigorous, moderate, and nonexercise groups. The risk of diabetes was reduced by 49% (RR, 0.51; 95% CI, 0.27-0.94;  $P = .01$ ) in the vigorous aerobic exercise group and by 53% (RR, 0.47; 95% CI, 0.25-0.89;  $P = .01$ ) in the moderate aerobic exercise group compared with the nonexercise group (Table 2). Likewise, similar results of moderate and vigorous aerobic exercise were observed in participants who completed 12-month intervention. Meanwhile, HbA<sub>1c</sub> and waist circumference was significantly reduced in the vigorous and moderate exercise groups compared with nonexercise group, and fasting plasma glucose level and weight regain appeared

lower in the exercise groups than the nonexercise group, although significant difference was not detected.

**Discussion** | In this randomized clinical trial, the data demonstrated that 12-month vigorous or moderate aerobic exercise programs could produce a long-term beneficial effect on diabetes prevention in individuals with central obesity. Although the Da Qing,<sup>2</sup> Finnish Diabetes Prevention Study,<sup>3</sup> and Diabetes Prevention Program<sup>1</sup> trials yielded beneficial results of lifestyle intervention for prevention of diabetes, these trials were exercise combined with diet, included individualized or group consulting, and involved individuals with impaired glucose tolerance.<sup>1-3</sup> In the current trial, the exercise programs during 1-year intervention were strictly coached and supervised, and all participants were instructed not to change their diet. Our main limitation is that incident diabetes was not prespecified, and some residual confounding may still be present, though we have performed multivariable regression analyses. Regarding the importance of obesity management in the prevention of type 2 diabetes addressed by the latest American Diabetes Association guideline,<sup>6</sup> our results are supportive of physical exercise as an effective scheme for obesity management to delay the progression of type 2 diabetes, and vigorous and moderate aerobic exercise programs could be implemented for prevention of type 2 diabetes in people with obesity.

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