ORIGINAL RESEARCH



Physical Activity Levels and Diabetes Prevalence in US Adults: Findings from NHANES 2015–2016

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ABSTRACT

Introduction: Diabetes is a major public health problem that is strongly influenced by lifestyle-related factors, with previous epidemiologic studies finding an inverse relationship between physical activity and the prevalence of diabetes. We aimed to quantify the prevalence of diabetes and determine whether a dose-response relationship is present between physical activity levels and diabetes.

Methods: Population characteristics were compared between diabetic and nondiabetic

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Department of Neurology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, China subjects. Multiple logistic regression models were used to assess the association between different levels of physical activity and diabetes. Restricted cubic spline analysis was used to examine the dose-response relationship between physical activity and diabetes prevalence.

Results: Compared with those in the lowest physical activity quartile, participants in the highest quartile had a 42% lower prevalence of diabetes (odds ratio = 0.58, 95% confidence interval = 0.44–0.75, p < 0.001). A nonlinear dose-response relationship was observed (p nonlinearity < 0.05), with increased physical activity associated with a decreased prevalence of diabetes, with steeper reductions in the prevalence of diabetes at low activity levels than at high activity levels. These results were robust in both subgroup and sensitivity analyses.

Conclusions: Higher levels of physical activity are associated with a lower prevalence of diabetes. The data indicated the presence of a nonlinear dose-response relationship in all of the included subjects, with steeper reductions in the prevalence of diabetes at low activity levels than at high activity levels. Increasing physical activity is therefore potentially a useful intervention for reducing the prevalence of diabetes.

Keywords: Association; Diabetes; Physical activity; Restricted cubic spline

Key Summary Points

Previous epidemiologic studies found an inverse relationship between physical activity and the risk of diabetes

We aimed to quantify the risk of diabetes and determine whether a dose-response relationship is present between physical activity levels and diabetes

The study showed that there was a nonlinear dose-response relationship in the included subjects. Steeper reductions in the diabetes risk were seen at low activity than at high activity

The study indicated that increasing physical activity may be a useful intervention to reduce the diabetes

INTRODUCTION

Diabetes is one of the most-common metabolic disorders and emerges as a secondary outcome because of interactions among genetic, environmental, and lifestyle factors [1]. It requires continuous, multidisciplinary medical care, combined with patient self-management, family support, and education to prevent or delay morbidity and mortality in end organs [2]. The disease affects almost every organ system in the body and is often accompanied by complications such as blindness, renal failure, heart disease, strokes, and foot ulcers [3]. Global statistics indicate that approximately 382 million people worldwide were suffering from this disease in 2012 and 2013, with diabetes causing 1.5-5.1 million deaths annually, ranking it as the eighth leading cause of death worldwide [4]. As a major public health problem, the prevalence of diabetes is increasing rapidly worldwide. The International Diabetes Federation has predicted that by 2035 the number of people with diabetes worldwide will increase to 592 million [5].

Diabetes is associated with a genetic predisposition but it is also strongly influenced by lifestyle-related factors such as diet and physical activity. Preventing diabetes through appropriate lifestyle changes is therefore an urgent health issue [6]. Many studies have investigated the relationship between physical activity and diabetes prevalence, with most finding an inverse association such that insufficient physical activity is a major risk factor for diabetes [7-10]; only a few studies have found no significant correlation [11].

Changes in lifestyles have an increasing impact on disease. On the one hand, many people have some unhealthy lifestyles due to work and study (sedentary, playing games online, watching TV, etc.). On the other hand, the whole population is attaching great importance to health, and many people have adopted a variety of physical activities. Many observational studies have demonstrated the effects of physical activity level on the prevalence of diabetes [12–14]. In the present study we performed comprehensive calculations of physical activities of different intensities and durations and analyzed the dose-response relationship between physical activity and the prevalence of diabetes. The specific purposes were to quantify the prevalence of diabetes and assess the possibility of a doseresponse relationship while addressing potential confounding. Providing quantitative estimates of dose-response relationships will be critical to estimating how changes in physical activity levels in the general population will affect disease incidence, thereby allowing more-detailed guidance to be provided to the general public. This study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving research study participants were approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB) [Protocol #2011-17]. Written informed consent was obtained from all participants.

METHODS

Study Population

This retrospective cross-sectional study analyzed data from the National Health and Nutrition Examination Survey performed in 2015 and 2016 (NHANES 2015–2016). The NHANES is a continuous annual survey conducted by the National Center for Health Statistics (NCHS) that combines interviews and physical examinations to assess the health and nutritional status of US adults and children. The NCHS institutional committee approved the NHANES, and subjects included in the survey participated voluntarily and signed informed consents. A detailed description of the survey design can also be found on the NHANES website [15]. The analysis performed in the present study was limited to adults aged \geq 20 years with no missing information for the variables of interest and involved the cross-sectional analysis of 3932 participants in NHANES 2015–2016.

Definition of Outcome

Diabetes patients were identified based on both laboratory and personal interview data. We defined the diabetes status of the participants as follows based on the American Diabetes Association guideline, using the measured HgbA1c as a diagnostic criterion: no diabetes treatment (e.g., taking insulin or oral hypoglycemic agents to lower blood glucose levels); participants with HgbA1c < 6.5% and $\geq 6.5\%$ would be categorized as having no diabetes and diabetes, respectively. We also excluded participants with a family history of diabetes and included additional participants based on a positive answer to the following question: Have you ever been told by a doctor or health professional that you have diabetes?

Evaluation of Exposure

Physical activity was reported using a physical activity questionnaire based on the Global Physical Activity Questionnaire, which provides respondent-level interview data on physical activity. Physical activity was divided into the following five types: vigorous work activity, moderate work activity, walking or bicycling, vigorous recreational activity, and moderate recreational activity. The duration of physical activity was calculated by multiplying the numbers of days of a specific activity performed per week (in days/week) by the duration of the specific activity per day (in minutes/day) to produce metabolic equivalent scores (METs, in minutes/week). In this way we quantified the estimated physical activity level exposure using METs as a common unit to make it possible to integrate activities with different intensities and durations performed during each week.

Population Covariates

We extracted demographic characteristics including gender, age, race, educational level, marital status, BMI (body mass index), depressive state, and poverty as potential covariates.

Age was divided into three groups: 20-44 years, 45-64 years, and 65-80 years. There were five race groups, which were based on those used in the NHANES questionnaire: Mexican-American, other Hispanic, non-Hispanic white, non-Hispanic black, and other race. Educational level was categorized into three groups: < 9th grade education, 9-11th grade education, and college graduate or higher. Marital status was grouped into the three categories of unmarried, married, and other (divorced, separated, or widowed). BMI was quantified as the body weight in kilograms divided by the height in meters squared and defined as underweight ($< 18.5 \text{ kg/m}^2$), normal (18.5–24.9 kg/m²), overweight (25–29.9 kg/ m^2), or obese (> 30 kg/m²) based on the WHO International BMI Classification criteria for adults. We used a depression screening questionnaire to obtain a total score for the severity of depression, with a depressive state then assessed using predefined cutoff points into either "yes" for a score ≥ 5 and "no" for a score < 5. The INDFMMPI (family monthly poverty level index) based on the monthly income was used to determine whether poverty is present. The cutoff for poverty being present was determined by whether the INDFMMPI of a family was less than the poverty threshold, which is represented by a ratio of 1; we therefore defined this as "yes" for INDFMMPI ≤ 1 and "no" for INDFMMPI > 1.

Statistical Analysis

All analyses in this study were conducted using Stata software (version 14.0). The population characteristics of the study sample were first compared with the diabetes status, by

examining differences in demographic variables using the *t*-test for continuous variables and Pearson's chi-square test for categorical variables. Multiple logistic regression was then used to determine the association between the different physical activity levels and diabetes. Three models were evaluated: (1) unadjusted associations were first examined. (2) then these associations were adjusted for age and race, and (3) they were adjusted for educational level, marital status, BMI, depressive state, and poverty. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to demonstrate the strength and direction of each association. Lastly, we used restricted cubic spline (RCS) analysis to assess the dose-response relationship between physical activity and diabetes prevalence with four knots at the 25th, 50th, 75th, and 95th percentiles of physical activity levels, and an RCS map was drawn.

Subgroup and Sensitivity Analyses

We finally performed detailed subgroup and sensitivity analyses of the relationship of physical activity to diabetes prevalence. A multiple logistic regression analysis was used to stratify the data by gender to analyze the impact of gender differences on the link between physical activity and diabetes. We also observed the dose-response relationship between physical activity and diabetes for different gender, age, and race groups. Due to the large amount of missing data for depressive state and poverty, a cross-sectional analysis that excluded these covariates was conducted as a sensitivity analysis involving 4600 participants.

All tests were two-tailed, and a probability values of p < 0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

The baseline parameters for the demographics, lifestyle habits, and living conditions of cases and controls are presented in Table 1.

Application of the inclusion criteria resulted in 3932 subjects from NHANES 2015-2016 being enrolled in this study, of which 48.78% were male. The percentage of subjects with diabetes was 18.64%, and the average of physical activity levels in the diabetic and nondiabetic participants were 2291.63 METs and 3734.11 METs, respectively. Table 1 indicates that the gender distribution did not differ between the subjects with and without diabetes. Older subjects and blacks were more likely to have diabetes. The diabetic subjects were more likely to be married and have a lower level of education compared with the nondiabetic subjects. The prevalence rates of having higher BMI, depression, and poverty, and fewer physical activities per week were higher among the diabetic subjects.

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Multiple Logistic Regression Analysis of Physical Activity and Diabetes

Table 2 presents the results obtained from the multiple logistic regression models, in which diabetes was the main outcome variable and the level of physical activity was the main predictor after adjusting for age, race, educational level, marital status, BMI, depressive state, and poverty. Among all of the participants, the prevalence of diabetes was significantly lower in the high-physical-activity group than in the low-physical-activity group after adjusting for covariates.

Specifically, the prevalence of diabetes was 29%, 34%, and 42% lower among participants in the second, third, and fourth quartiles of physical activity compared with those in lowest physical activity quartile (odds ratios [ORs] = 0.71, 0.66, and 0.58, respectively; 95% confidence intervals [CIs] = 0.56–0.89, 0.52–0.84, and 0.44–0.75; p < 0.01, p < 0.01, and p < 0.001).

Dose-Response Relationship Between Physical Activity and Diabetes Prevalence

RCS regressions were performed to examine the associations between physical activity levels and the prevalence of diabetes. An RCS function with four knots located at the 25th, 50th, 75th, and 95th percentiles was used for physical

Characteristic	Diabetes	Non-diabetes	χ^2/t	p value*
Participants	733 (18.64)	3199 (81.36)		
Gender				
Male	377 (51.43)	1541 (48.17) 2.54		0.111
Female	356 (48.57)	1658 (51.83)		
Age (years)				
20-44	111 (15.14)	1545 (48.30)	303.23	< 0.001
45-64	316 (43.11)	1036 (32.39)		
65-80	306 (41.75)	618 (19.31)		
Race				
Mexican American	170 (23.19)	517 (16.16)	40.34	< 0.001
Other Hispanic	103 (14.05)	402 (12.57)		
Non-Hispanic White	211 (28.79)	1222 (38.20)		
Non-Hispanic Black	164 (22.37)	595 (18.60)		
Other race	85 (11.60)	463 (14.47)		
Education level				
Less than 9th grade education	233 (31.79)	627 (19.60) 54.23		< 0.001
9–11th grade education	157 (21.42)	715 (22.35)		
College graduate or higher	343 (46.79)	1857 (58.05)		
Marital status				
Unmarried	78 (10.64)	616 (19.26)	30.76	< 0.001
Married	415 (56.62)	1607 (50.23)		
Other	240 (32.74)	976 (30.51)		
BMI (kg/m ²)				
< 18.5	4 (0.54)	49 (1.53)	173.65	< 0.001
18.5–24.9	79 (10.78)	883 (27.60)		
25–29.9	196 (26.74)	1089 (34.04)		
≥ 30	454 (61.94)	1178 (36.83)		
Depressive state				
Yes	241 (32.88)	777 (24.29)	22.93	< 0.001
No	492 (67.12)	2422 (75.71)		
Poverty				
Yes	226 (30.83)	728 (22.76)	21.16	< 0.001

507 (69.17)

No

2471 (77.24)

Table 1 Population characteristics by diabetes status in NHANES 2015 to 2016 (N = 3932)

Table 1 continued

Characteristic	Diabetes	Non-diabetes	χ^2/t	p value*
Physical activity (METs)	2291.63	3734.11	57.72	< 0.001

Data are presented as n (%) or mean

NHANES National Health and Nutrition Examination Survey, *BMI* body mass index, *MET* metabolic equivalents **p* value for comparison of difference in proportion between diabetic and nondiabetic subjects, using *t*-test for continuous variables and Pearson's chi-square test for categorical variables

Physical activity	Total participants			
	OR	95% CI	p value	
Model I ^a				
Q1	1			
Q2	0.64	0.52-0.79	< 0.001	
Q3	0.47	0.38-0.59	< 0.001	
Q4	0.37	0.30-0.46	< 0.001	
Model II ^b				
Q1	1			
Q2	0.71	0.57-0.88	0.002	
Q3	0.61	0.48-0.77	< 0.001	
Q4	0.54	0.42-0.69	< 0.001	
Model III ^c				
Q1	1			
Q2	0.71	0.56-0.89	0.003	
Q3	0.66	0.52-0.84	0.001	
Q4	0.58	0.44-0.75	< 0.001	

Table 2 ORs and 95% CI for the relation between thediabetes and physical activity in NHANES 2015 to 2016

OR odds ratio, *CI* confidence interval, *NHANES* National Health and Nutrition Examination Survey

^a Model I only comparing diabetes to physical activity

^b Model II adjusted for baseline gender, age, and race

^c Model III adjusted for baseline gender, age, race, education level, marital status, BMI, depressive state, and poverty

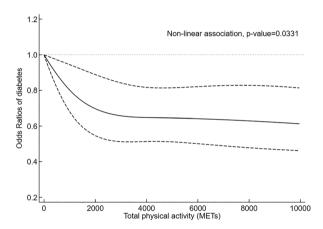


Fig. 1 Dose-response relationships between total physical activity (METs min/day) and the prevalence of diabetes in 3932 adults of NHANES 2015–2016. This graph shows ORs (solid line) with 95% CI (dashed lines). Models are adjusted for gender, age, race, education level, marital status, BMI, depressive state, and poverty. Total physical activity was modeled by unrestricted cubic splines with four knots at percentiles 25%, 50%, 75%, and 95% in a generalized logistic regression model. The reference value is 0 METs (p nonlinearity < 0.05)

activity levels in the regression analyses. Figure 1 shows the dose-response relationship between total physical activity and the prevalence of diabetes in the overall sample.

The spline model analysis also revealed a nonlinear dose-response relationship between physical activity and diabetes in the general population (p nonlinearity < 0.05), with steeper reductions in the prevalence of diabetes at low activity levels than at high activity levels. The prevalence of diabetes was 13% lower in participants with a physical activity level of 600

METs (the minimum recommended level) than in those with no physical activity (OR = 0.87, 95% CI = 0.78–0.97). The prevalence of diabetes decreased rapidly as the physical level increased from 0 to 2000 METs, while it decreased more slowly for physical levels above 2000 METs. The point estimate of the risk ratio reached 0.80 (95% CI = 0.68–0.95) for activity at 980 METs, indicating that the probability of having diabetes was 20% lower at that level of physical activity.

Subgroup and Sensitivity Analyses

Considering gender difference in physical activity, Table 3 lists the results from the multiple logistic regression models stratified by gender. Female participants showed the same correlation as for all of the participants, with ORs of 0.67, 0.63, and 0.51 for those in the second, third, and fourth quartiles of physical activity, respectively, compared with the lowest

physical activity quartile (95% CI = 0.47–0.94, 0.44–0.89, and 0.35–0.73, respectively; p < 0.05, p < 0.01, and p < 0.001). Among the male participants, the prevalence of diabetes was 34% lower for those in the fourth quartile of physical activity than in the lowest physical activity quartile (OR = 0.66, 95% CI = 0.45–0.95, p < 0.05), with no significant relationships in the other quartile groups.

In the gender-stratified analyses, a similar nonlinear dose-response relationship was observed in females (*p* nonlinearity < 0.05), with a more significant reduction in prevalence at low levels of activity than at high levels (Fig. 2b), and increased physical activity being associated with a decreased prevalence of diabetes. The prevalence of diabetes was 25% lower in females with a physical activity level of 600 METs than in females with no physical activity (OR = 0.75, 95% CI = 0.60–0.92). No significant relationship was found in males.

Physical activity	Male participants			Female]	Female participants		
	OR	95% CI	p value	OR	95% CI	p value	
Model I ^a	1			1			
	0.75	0.56-1.01	0.057	0.64	0.46-0.87	0.005	
	0.45	0.32-0.62	< 0.001	0.45	0.33-0.62	< 0.001	
	0.38	0.27-0.53	< 0.001	0.39	0.28-0.54	< 0.001	
Model II ^b	1			1			
	0.86	0.63-1.18	0.355	0.67	0.49-0.93	0.017	
	0.63	0.45-0.88	0.008	0.60	0.43-0.83	0.002	
	0.63	0.44-0.90	0.010	0.53	0.38-0.75	< 0.001	
Model III ^c	1			1			
	0.87	0.63-1.20	0.385	0.67	0.47-0.94	0.022	
	0.71	0.50-1.01	0.057	0.63	0.44-0.89	0.009	
	0.66	0.45-0.95	0.025	0.51	0.35-0.73	< 0.001	

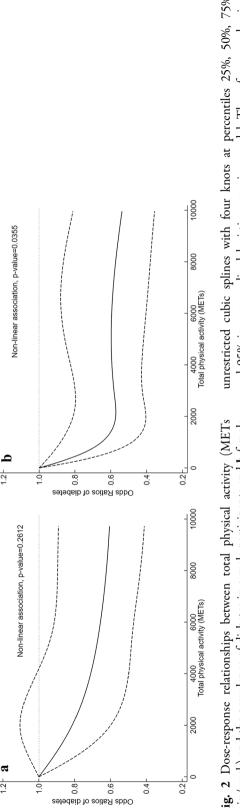
Table 3 ORs and 95% CI for the relation between the diabetes and physical activity in males and females

OR odds ratio, CI confidence interval, NHANES National Health and Nutrition Examination Survey

^a Model I only comparing diabetes to physical activity

^b Model II adjusted for baseline age and race

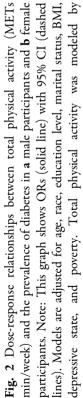
^c Model III adjusted for baseline age, race, education level, marital status, BMI, depressive state, and poverty



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1.2



unrestricted cubic splines with four knots at percentiles 25%, 50%, 75%, and 95% in a generalized logistic regression model. The reference value is 0 METs. Nonlinear dose-response relationship was observed in (b) female participants (p nonlinearity < 0.05); there was no significant relationship in males

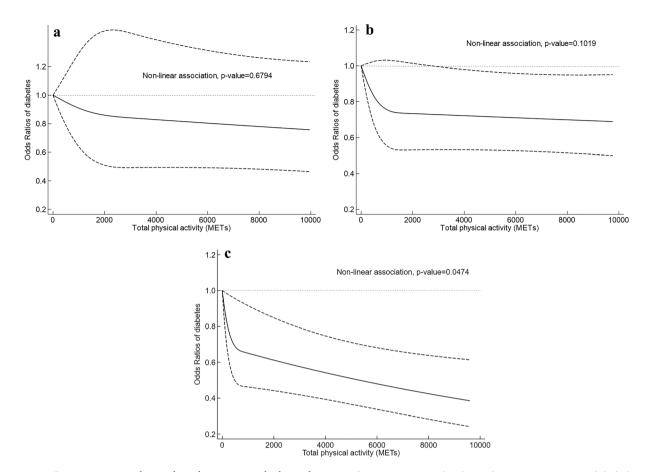


Fig. 3 Dose-response relationships between total physical activity (METs min/week) and the prevalence of diabetes in a 20–44-year-old, b 45–64-year-old, and c 65–80-year old participants. This graph shows ORs (solid line) with 95% CI (dashed lines). Models are adjusted for gender, race, education level, marital status, BMI, depressive state,

In the age-stratified analyses, a nonlinear dose-response relationship was observed in those aged 65–80 years (p nonlinearity < 0.05), with no significant relationship in the other groups (Fig. 3). In the race-stratified analyses we observed a nonlinear dose-response in the other Hispanic and non-Hispanic white group (p nonlinearity < 0.05), with no significant relationship in the other groups (Fig. 4). All of the dose-response relationships demonstrated an inverse relationship between physical activity levels and the prevalence of diabetes.

Sensitivity cross-sectional analyses that excluded subjects with a depressive state and poverty yielded similar results. The nonlinear

and poverty. Total physical activity was modeled by unrestricted cubic splines with three knots at percentiles 20%, 40%, and 60% in a generalized logistic regression model. The reference value is 0 METs. Nonlinear doseresponse relationship was only observed in (c) the 65–80year-old group (*p* nonlinearity < 0.05)

dose-response relationship between physical activity (*p* nonlinearity < 0.01) and diabetes and the point estimate of the risk ratio reached 0.80 (95% CI = 0.70–0.92) at 900 METs of activity, with the reduction in prevalence being slightly more pronounced at low physical activity levels than at high levels (Fig. 5).

DISCUSSION

This retrospective cross-sectional study combined interviews and physical examinations of subjects living in the US to analyze the prevalence of diabetes. We observed that patients

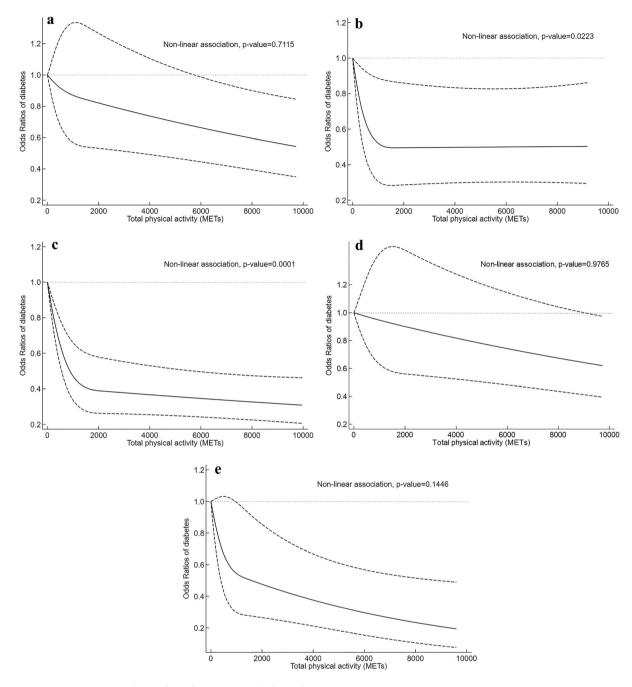


Fig. 4 Dose-response relationships between total physical activity (METs min/week) and the prevalence of diabetes in a Mexican American, b Other Hispanic, c Non-Hispanic White, d Non-Hispanic Black, and e Other Race participants. This graph shows ORs (solid line) with 95% CI (dashed lines). Models are adjusted for gender, age, education level, marital status, BMI, depressive state, and

poverty. Total physical activity was modeled by unrestricted cubic splines with three knots at percentiles 20%, 40%, and 60% in a generalized logistic regression model. The reference value is 0 METs. Non-linear dose-response relationships were observed in **b** the Other Hispanic and **c** Non-Hispanic White group (p nonlinearity < 0.05)

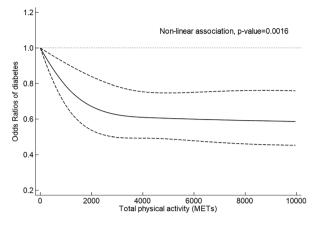


Fig. 5 Dose-response relationships between total physical activity (METs min/day) and the prevalence of diabetes in 4600 adults of NHANES 2015–2016. This graph shows ORs (solid line) with 95% CI (dashed lines). Models are adjusted for age, race, education level, marital status, and BMI. Total physical activity was modeled by unrestricted cubic splines with four knots at percentiles 25%, 50%, 75%, and 95% in a generalized logistic regression model. The reference value is 0 METs (*p* nonlinearity < 0.01)

with diabetes were older than nondiabetic subjects, with an increased prevalence of diabetes being very common in the elderly [16]. The personal and economic cost of diabetes in the elderly has become a significant burden in the US. For example, the American Diabetes Association reported that 59% of healthcare expenditure for diabetes in the US in 2012 was spent on patients > 65 years old [17]. The present results further indicate that diabetics patients tend to be less educated, which is consistent with the findings for other developed countries [18]. The increased prevalence of diabetes among subjects with a lower education may be due to people with higher education being more likely to be knowledgeable about health promotion and exhibit health-promoting behaviors. We also found that diabetes was more prevalent among patients suffering from poverty and depression, implying that people on low incomes might have worse access to healthcare resources and high-quality diabetes care [19]. There also needs to be a focus on mental health services provided to diabetic patients [20]. The increasing burden of diabetes indicates the need for studies focusing on lifestyle recommendations and improved treatments for the risk factors affecting people at a high prevalence of diabetes.

This study explored the relationship between physical activity and diabetes and also performed subgroup analyses with adjustment for confounding factors (e.g., gender, age, and race) as well as sensitivity analyses. We observed a dose-response relationship between physical activity and the prevalence of diabetes, with the results indicating that physical activity was significantly and inversely associated with an increased prevalence of diabetes after adjusting for potential confounders. This was consistent with the findings of previous studies that investigated the relationship between physical activity and diabetes [21-23]. Meanwhile, the present results did no change substantially in subgroup and sensitivity analyses. The consistency of the obtained evidence for a dose-response relationship and the stability of results in various subgroup and sensitivity analyses all point to the relationship between increased physical activity and a reduced prevalence of diabetes. The current study also clearly found a nonlinear dose-response relationship between physical activity and diabetes in the general population, with steeper reductions in the prevalence of diabetes at low activity levels than at high activity levels, with consistent results obtained in the sensitivity analysis.

It is worth noting that in the subgroup analysis, significant nonlinear dose-response relationships were observed only among the female subjects and those aged 65–80 years. This suggests that moderate increases in physical activity in females and the elderly is more beneficial for reducing the prevalence of diabetes. Insulin action or sensitivity declines with age, leading to impaired glucose tolerance, and these effects can be reduced by maintaining a physically active lifestyle [24]. These observations should be further confirmed.

Several biologic mechanisms could explain the link between physical activity and diabetes. Physical activity improves the energy balance and can prevent obesity [23], while obesity is an independent risk factor for diabetes [25]. However, we found that the risk can be reduced even after adjusting for differences in BMI. Several other mechanisms might explain the impact of physical activity on the prevalence of diabetes regardless of obesity. For example, physical activity can directly reduce the blood glucose level and increase insulin sensitivity [26]. In addition, long-term physical activity leads to many adaptations in skeletal muscle, including increased mitochondrial activity and content, changes in the types of muscle fibers, and increased expression of the GLUT4 protein, which may contribute to reducing the diabetes prevalence [27].

We further found that a 980-MET increase in physical activity produced a 20% reduction in the prevalence of diabetes. This level of physical activity corresponds to either running at 6 km per hour for 30 min or walking briskly at 5.2 km per hour for 60 min on 5 days per week. Increasing physical activity is therefore potentially an effective intervention for reducing prevalence of diabetes. Meanwhile, we also found that a 20% reduction in the prevalence of diabetes corresponded to a 2240-MET increase in physical activity of males and 440-MET of females; therefore, different physical activity standards can be developed for males and females. Our findings have important public health implications, since adopting and maintaining physical activity are critical for health promotion.

Our study had some considerable strengths. First, the study participants come from a large representative national survey, which increased the statistical power of the findings. Moreover, after adjusting for several confounding factors, we performed a multiple logistic regression analysis and still observed the protective effect of physical activity on diabetes, indicating the stability of our results. We also conducted detailed subgroup and sensitivity analyses, which produced robust results. In addition, all body parameters in this study were measured by trained health technicians using standard measurement procedures, further increasing the accuracy of the research results. Finally, we removed diabetic patients by applying criteria such as taking oral hypoglycemic agents or insulin, and so the cases included in our study samples were generally new cases, which reduces recall bias.

We acknowledge that this study was subject to some limitations. First, although our multiple models adjusted for the effects of important confounders, causal relationships could not be established because both the exposure (physical activity) and outcome (diabetes) indicators were collected concurrently. Therefore, causality still needs to be analyzed in large-scale cohort studies. Second, all of the data were obtained and verified using simple self-report questions, which are not as accurate as biometric measurements and are likely to introduce recall bias. Lastly, the present findings might not be applicable to other countries, including other Asian ones.

CONCLUSION

The present findings provide clear scientific evidence that higher levels of physical activity are associated with a lower prevalence of diabetes. The nonlinear dose-response relationship in all of the included subjects showed steeper reductions in the prevalence of diabetes at low activity levels than at high activity levels.

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Authorship Contributions. Fanfan Zhao and Wentao Wu contributed equally to this work.

Compliance with Ethics Guidelines. This study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving research study participants were approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB) [Protocol #2011-17]. Written informed consent was obtained from all participants.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

1. Sliwinska-Mosson M, Milnerowicz H. The impact of smoking on the development of diabetes and its complications. Diabetes Vasc Dis Res. 2017;14(4): 265–76.

- 2. American DA. Standards of medical care in diabetes–2010. Diabetes Care. 2010;33(Suppl 1): S11–61.
- Krishnan B, Babu S, Walker J, Walker AB, Pappachan JM. Gastrointestinal complications of diabetes mellitus. World J Diabetes. 2013;4(3):51–63.
- 4. Tao Z, Shi A, Zhao J. Epidemiological perspectives of diabetes. Cell Biochem Biophys. 2015;73(1): 181–5.
- 5. Shi Y, Hu FB. The global implications of diabetes and cancer. Lancet. 2014;383(9933):1947–8.
- 6. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Eng J Med. 2002;346(6):393–403.
- 7. Burchfiel CM, Sharp DS, Curb JD, et al. Physicalactivity and incidence of diabetes—the honolulu heart program. Am J Epidemiol. 1995;141(4):360–8.
- Njolstad I, Arnesen E, Lund-Larsen PG. Sex differences in risk factors for clinical diabetes mellitus in a general population: a 12-year follow-up of the Finnmark Study. Am J Epidemiol. 1998;147(1): 49–58.
- Carlsson S, Midthjell K, Tesfamarian MY, Grill V. Age, overweight and physical inactivity increase the risk of latent autoimmune diabetes in adults: results from the Nord-Trondelag health study. Diabetologia. 2007;50(1):55–8.
- 10. Wahid A, Manek N, Nichols M, et al. Quantifying the association between physical activity and cardiovascular disease and diabetes: a systematic review and meta-analysis. J Am Heart Assoc. 2016;5(9):e002495.
- 11. Waki K, Noda M, Sasaki S, et al. Alcohol consumption and other risk factors for self-reported diabetes among middle-aged Japanese: a population-based prospective study in the JPHC study cohort I. Diabet Med. 2005;22(3):323–31.
- 12. Weinstein AR, Sesso HD, Lee IM, et al. Relationship of physical activity vs body mass index with type 2 diabetes in women. JAMA. 2004;292(10):1188–94.
- 13. Lynch J, Helmrich SP, Lakka TA, et al. Moderately intense physical activities and high levels of cardiorespiratory fitness reduce the risk of non-insulindependent diabetes mellitus in middle-aged men. Arch Intern Med. 1996;156(12):1307–14.
- Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS. Physical-activity and reduced occurrence of non-insulin-dependent diabetes-mellitus. New Engl J Med. 1991;325(3):147–52.

- 15. Services USDoHaH. Center for Disease Control and Prevention National Health and Nutrition Examination Survey. https://www.cdc.gov/nchs/nhanes. htm. Accessed 6 Nov 2015.
- 16. Fagot-Campagna A, Bourdel-Marchasson I, Simon D. Burden of diabetes in an aging population: prevalence, incidence, mortality, characteristics and quality of care. Diabetes Metab. 2005;31 Spec No 2:5S35–5S52.
- 17. Sircar M, Bhatia A, Munshi M. Review of hypoglycemia in the older adult: clinical implications and management. Can J Diabetes. 2016;40(1): 66–72.
- 18. Blomster JI, Zoungas S, Woodward M, et al. The impact of level of education on vascular events and mortality in patients with type 2 diabetes mellitus: results from the ADVANCE study. Diabetes Res Clin Pract. 2017;127:212–7.
- 19. Seddon ME, Marshall MN, Campbell SM, Roland MO. Systematic review of studies of quality of clinical care in general practice in the UK, Australia and New Zealand. Qual Health Care. 2001;10(3): 152–8.
- 20. Wang KX, Li FN, Cui YX, et al. The association between depression and type 1 diabetes mellitus: inflammatory cytokines as ferrymen in between? Mediat Inflamm. 2019;1–11.
- 21. Meisinger C, Lowel H, Thorand B, Doring A. Leisure time physical activity and the risk of type 2 diabetes

in men and women from the general population. The MONICA/KORA Augsburg Cohort Study. Diabetologia. 2005;48(1):27–34.

- 22. Rana JS, Li TY, Manson JE, Hu FB. Adiposity compared with physical inactivity and risk of type 2 diabetes in women. Diabetes Care. 2007;30(1):53–8.
- 23. Lee DC, Park I, Jun TW, et al. Physical activity and body mass index and their associations with the development of type 2 diabetes in Korean men. Am J Epidemiol. 2012;176(1):43–51.
- 24. Wang JT, Ho LT, Tang KT, Wang LM, Chen YD, Reaven GM. Effect of habitual physical activity on age-related glucose intolerance. J Am Geriatr Soc. 1989;37(3):203–9.
- 25. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in diet and lifestyle and long-term weight gain in women and men. New Engl J Med. 2011;364(25):2392–404.
- Mayer-Davis EJ, D'Agostino R, Karter AJ, et al. Intensity and amount of physical activity in relation to insulin sensitivity—the Insulin Resistance Atherosclerosis Study. Jama J Am Med Assoc. 1998;279(9):669–74.
- 27. Rockl KSC, Witczak CA, Goodyear LJ. Signaling mechanisms in skeletal muscle: Acute responses and chronic adaptations to exercise. IUBMB Life. 2008;60(3):145–53.