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OPEN Comparative study on the association between types of physical activity, physical activity levels, and the incidence of osteoarthritis in adults: the NHANES 2007–2020

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It is known that physical activity is beneficial for the prevention of osteoarthritis (OA), but specific discussions on which types and levels of physical activity are more effective in reducing the incidence of OA are restricted. This study is aimed at exploring the correlation concerning the types of physical activity, levels of physical activity, and the incidence of OA by assessing the participation in five typical forms of physical activity (vigorous work activity, vigorous recreational activity, moderate work activity, moderate recreational activity, and walking or bicycling). Cross-sectional study was conducted. Self-reported data on specific types of physical activity were obtained from individuals in the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2020 with the use of the Physical Activity Questionnaire (PAQ). The incidence of OA was assessed through the "Health Conditions" questionnaire section of NHANES. Weighted logistic regression analysis was employed to study the correlation between physical activity types and levels, and the incidence of OA. Different kinds of physical activity and physical activity levels have varying impacts on the incidence of OA. Among the types of physical activity, vigorous recreational activity and moderate recreational activity are found to have a preventive effect on OA. In terms of physical activity levels, low physical activity levels of moderate work activity are associated with an increased risk of OA, while moderate physical activity levels are confirmed to have a protective effect against OA in the age groups of 20-44 and 45-64. However, gender-stratified analyses reveal that both low and moderate physical activity levels provide protection against OA in males, with moderate physical activity levels showing a more significant protective effect.

Keywords Osteoarthritis, Physical activity, Epidemiology, NHANES

Abbreviations

BMI	Body mass index
CI	Confidence interval
MET	Metabolic equivalent
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio
PAQ	Physical Activity Questionnaire

¹Orthopedics Department, The First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin 300000, People's Republic of China. ²National Clinical Research Center for Chinese Medicine Acupuncture and Moxibustion, Tianjin 300000, People's Republic of China. ³The Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin, China. ⁴Binhai New Area Traditional Chinese Medicine Hospital, Tianjin, China. ⁵These authors contributed equally: Chenyang Huang and Ziyu Guo. ^{III}email: 569481804@qq.com; gu840134@163.com Osteoarthritis (OA) refers to one of the most common joint diseases worldwide, influencing around 10% of men and 18% of women over 60 years of age¹. it can occur in both large and small joints throughout the body, with the primary manifestations including morning stiffness, pain, deformity and joint activity limitations, and in severe cases, it can lead to joint instability or limb disability, seriously impacting quality of life².

Epidemiological studies have indicated that physical activity is closely related to OA³. Based on different activity types, physical activity types can be categorized into occupational activity, recreational activity, and transportation activity. Additionally, different physical activity levels can be calculated based on various factors such as activity intensity, frequency, duration, and type. Most previous studies consistently revealed that physical activity can lower the risk of developing OA in joints. However, during physical activity, the load on the joints of the human body increases, and different types of physical activity impose varying loads on the knees ^{4,5}. The study found that when examining overall physical activity, the risk of OA did not increase⁶. One cohort study suggested that all kinds of physical activity are protective against knee OA^{7–9}. However, in a recent study from a university, it was found that low-to-moderate physical intensity of activity is protective for OA¹⁰, while high-intensity physical intensity of activity provides no protection against OA¹¹.

While many studies indicate that an active lifestyle can reduce the risk of OA, several studies have found that leisure physical activity and occupational physical activity have different effects on OA ¹²⁻¹⁴. Additionally, there is no definitive evidence supporting recommendations regarding physical activity types and levels. As a result, according to the National Health and Nutrition Examination Survey (NHANES) data in the USA, this study aims to explore the relationships between physical activity types (vigorous work activity, vigorous recreational activity, moderate work activity, moderate recreational activity, walking or bicycling) and levels (non, low, medium, high) and the risk of OA. Clarifying the association between specific physical activity types and levels and OA risk will provide insights and thus guide more targeted physical activity recommendations for OA prevention and management. The findings are conducive to informing and optimizing public health strategies to reduce the personal and socioeconomic burden of OA.

Materials and methods Study population

National Health and Nutrition Examination Survey (NHANE), a nationally representative cross-sectional survey conducted by the Centers for Disease Control and Prevention in the United States, employs a stratified, multi-stage random sampling method. The data analyzed in this study span the years 2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, 2017-2018, and the ongoing period of 2017-2020.Among the 56,171 participants in NHANES from 2007 to 2020, rigorous assessments were conducted to ensure the integrity, consistency, and logical coherence of physical activity data. In this present study, a meticulous examination of the dataset led to the exclusion of individuals with missing, refused, or unknown information regarding physical activity, sedentary time, and durations exceeding 24 h (n = 24,376). Additionally, participants lacking, refusing, or with unknown covariate information (n = 8894). Ultimately, 22,901 participants remained with no missing or confounding information regarding key outcomes, exposures, or variables (Fig. 1).

Diagnosis of OA

OA diagnosis data was from the "Medical Conditions" questionnaire section of the NHANES. First of all, participants were asked if doctor ever said they had arthritis. If they answered "yes," they would be further asked to identify "which type of arthritis was it" (The arthritis was classified as OA, rheumatoid arthritis, psoriatic arthritis, and others based on NHANES questionnaire data).

Assessment of types of physical activity and levels of physical activity

The Global Physical Activity Questionnaire was used to collect respondent-level weekly physical activity information¹⁵. Physical activity levels were examined for three categories of physical activity participation: vigorous work activity/vigorous recreational activities, moderate work activity/moderate recreational activities, and walk/bicycle information. Vigorous work activity was defined as typical activity that induced significant increases in breathing or heart rate for at least 10 min continuously, such as hauling or lifting heavy weights, excavating, or building work. Vigorous recreational activities were characterized as high-intensity sports, fitness activities, or leisure activities that generate significant increases in respiration or heart rate, such as jogging or basketball. Moderate work activity was defined as any activity that induces minor increases in breathing or heart rate, such as brisk walking or carrying light burdens for at least 10 min continuously. Moderate leisure activities were defined as those that generate a slight rise in breathing or heart rate for at least 10 min continuously. Moderate leisure activities were defined as those that generate a slight rise in breathing or heart rate for at least 10 min continuously, such as brisk walking, biking, swimming, or volleyball. Walking or use of a bicycle was defined as a transportation to school/work or for shopping for at least 10 min continuously to get to and from places.

According to the World Health Organization (WHO) Analytical Guidelines, physical activity (PA) is converted into metabolic equivalent minutes (MET-min) per week for moderate to vigorous PA¹⁶. MET values vary by the type of exercise, and NHANES provides recommended MET values for each PA. PA is calculated based on the MET values, weekly frequency, and duration of each PA using the formula: PA (MET-min/week) = MET × weekly frequency × duration¹⁷. A PA value of 0 indicates participants who are not engaged in any PA. Finally, the participants were classified into different groups based on their PA level. The groups were defined as NPA: Non-physical activity (0 MET-min/week), Low PA(LPA) (Q₁), Medium PA (MPA) (Q₂) and High PA (HPA) (Q₃)¹⁸.

Assessment of covariates

The following information was gathered using a household structured questionnaire: age (20–44, 45–64, ≥65 years), gender (male and female), race (Mexican American, Other Hispanic, Non-Hispanic white,

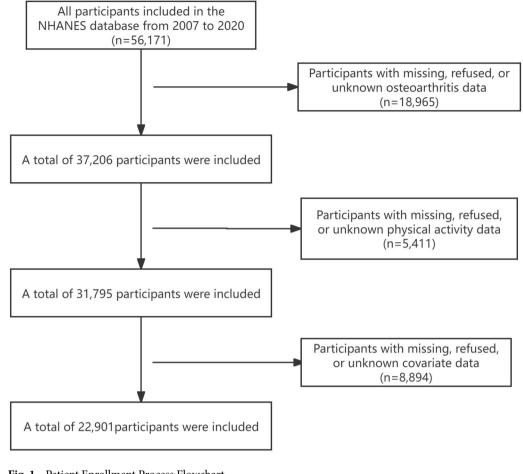


Fig. 1. Patient Enrollment Process Flowchart.

Non-Hispanic black and Other race), level of education (less than high school, high school, more than high school), Examination data included BMI (kg/m²). Laboratory data covered blood urea nitrogen (BUN, mmol/L)¹⁹, total calcium (Ca, mmol/L)²⁰, phosphorus (P, mmol/L)²¹, triglycerides (TG, mmol/L)²², uric acid (UA, μ mol/L)²³, and total cholesterol (TC, mmol/L)²⁴. As a final point, questionnaire data included information on smoking behavior (Yes/No)²⁵, alcohol consumption (Yes/No)²⁶, hypertension (Yes/No)²⁷, and diabetes (Yes/No)²⁸.

Statistical analysis

We used weighted samples and considered stratification and clustering in the design to generate nationally representative estimates for the US population. The NHANES cycles and weights were constructed according to the guidelines for continuous NHANES analysis²⁹. The participants' baseline characteristics were classified based on their physical activity level and OA status. A descriptive statistical analysis was performed on basic demographic information (age, gender, race, level of education), physical activity types (vigorous work activity, vigorous recreational activities, moderate work activity, moderate recreational activities, walk or bicycle, physical activity levels), body measurements (BMI), and diseases (hypertension, diabetes).Laboratory data included blood urea nitrogen, total calcium, phosphorus, triglycerides, uric acid, and total cholesterol. The categorical variables were reported in frequency (%), with the chi-square test for unordered categorical variables and the chi-square trend test for ordered multi-categorical variables.

STATA version 17.0 was used for statistical analysis (Stata Corp LP, College Station, TX, USA). R version 4.2.3 was used to create the forest graphs. A *p*-value under 0.05 was considered statistically significant.

Result

Among the 22,901 participants (41.5% male, 58.4% female), the overall prevalence of OA was 11.8%. Table 1 shows the baseline characteristics of the participants stratified by OA status. In general, OA was more common in middle-aged (45–64 years) and elderly (\geq 65 years) individuals, females and non-Hispanic whites. Higher education levels of above high school, BMI \geq 25 kg/m², heavy smoking, hypertension diagnosis and diabetes diagnosis were related to higher risk of OA. Compared to vigorous work activity and moderate work activity, OA prevalence was lower in those engaging in vigorous recreational activity and moderate recreational activity (Table 1). Females and participants with higher BMI were more likely to perform non-physical activity, and had higher risks of OA, hypertension or diabetes. Participants who received education higher than high school

Characteristic	Non-OA(n=20,196)	OA (n = 2705)	<i>p</i> -Value		
Age(years)					
20-44	7250(97.2)	206(2.8)	×0.007		
45-64	7331(87.5)	1049(12.5)	< 0.001		
≥65	5615(79.5)	1450(20.5)	1		
Gender					
Male	8669(91.2)	837(8.8)	< 0.001		
Female	11,527(86.1)	1868(13.9)	-		
Race	,	. ,			
Mexican American	3317(92.6)	250(7.4)	-		
Other Hispanic	2298(91.4)	216(8.6)	-		
Non-Hispanic white	7162(83.4)	1427(16.6)	< 0.001		
Non-Hispanic black	4810(89.4)	568(10.6)	-		
Other races	2809(92.0)	244(8.0)	-		
Level of education	2009(92.0)	211(0.0)			
<high school<="" td=""><td>5011(80.8)</td><td>671(10.2)</td><td>-</td></high>	5011(80.8)	671(10.2)	-		
< High school	5911(89.8) 4811(88.5)	671(10.2) 626(11.5)	< 0.001		
			-		
> High school	9474(89.1)	1408(12.9)			
BMI status(kg/m ²)	55 (0) 0)		-		
<25	5742(90.9)	551(9.1)	< 0.001		
≥25	14,724(87.2)	2154(12.8)			
Smoking status			< 0.001		
No	8681(86.1)	1399(13.9)			
Yes	11,515(89.8)	1306(10.2)			
Alcohol consumption					
Non-drinker	2939(89.1)	359(10.9)			
< 2 alcohol drinks	4293(85.2)	746(14.8)	< 0.001		
\geq 2 alcohol drinks	6902(90.8)	701(9.2)			
Unspecified	6062(87.1)	899(12.9)	1		
Hypertension					
Yes	7918(81.6)	1789(18.4)	< 0.001		
NO	12,278(93.1)	916(6.9)			
Diabetes					
Yes	3201(81.2)	743(18.8)	-		
NO	16,481(89.9)	1858(10.1)	<0.001		
Unspecified	514(83.2)	104(16.8)			
Vigorous work activity ^a					
Yes	19,504(88.0)	2656(12.0)	< 0.001		
NO	692(93.4)	49(6.6)			
Moderate work activity ^b		()			
Yes	17,540(88.4)	2305(11.6)	0.019		
NO	2656(86.9)	400(13.1)	0.019		
Walk or bicycle ^c	2030(00.7)	+00(13.1)			
1	17 574(97 9)	2453(12.2)	<0.001		
Yes	17,574(87.8)	2453(12.2)	< 0.001		
NO Visconsus as martine al estimited	2622(91.2)	252(8.8)			
Vigorous recreational activity ^d		a (15)	-		
Yes	19,149(87.8)	2657(12.2)	< 0.001		
NO	1047(95.6)	48(4.4)			
Moderate recreational activity ^e			-		
Yes	16,393(87.9)	2253(12.1)	0.008		
NO	3803(89.4)	452(10.6)			
Physical activity levels (met-h/week)					
0	9413(86.2)	1509(13.8)			
Q ₁ (1.4–17.1)	4265(89.3)	510(10.7)			
Q ₂ (17.7–42.9)	5335(90.7)	616(9.3)	< 0.001		
Q ₃ (45-1080)	2686(88.2)	251(11.8)	1		
Laboratory indices			1		
Continued		1	1		

Characteristic	Non-OA(n=20,196)	OA (n = 2705)	<i>p</i> -Value
Blood urea nitrogen (mmol/L)	4.93 ± 0.018	5.80 ± 0.058	< 0.001
Total calcium (mmol/L)	2.34 ± 0.001	2.34 ± 0.003	0.001
Phosphorus (mmol/L)	1.20 ± 0.002	1.22 ± 0.005	0.025
Triglycerides (mmol/L)	1.76±0.013	1.83 ± 0.034	0.017
Uric acid (µmol/L)	319.78±0.797	323.79±2.26	< 0.001
Total cholesterol (mmol/L)	5.28 ± 0.014	5.26 ± 0.039	< 0.001

Table 1. Baseline characteristics of the research population with and without OA. n: sample size; BMI, body mass index (calculated as weight in kilograms divided by height in square meters); MET, metabolic equivalent. ^aVigorous work activity: typical activity that induced signification increases in breathing or heart rate for at least 10 min continuously. ^bModerate work activity: any activity that induces minor increases in breathing or heart rate. ^cwalk or use a bicycle for at least 10 min continuously to get to and from places. ^dVigorous recreational activities: high-intensity sports, fitness activities, or leisure activities that generate signification increases in breathing or heart rate. ^cModerate recreational activities: any activity that generates a slight rise in breathing or heart rate for at least 10 min continuously. Continuous variables were presented by mean ± Standard error (SE), and categorical variables were presented with numbers and percentages.

tended to have low physical activity level. Those with lower BMI and non-whites were more likely to have medium physical activity level. Younger individuals (20–44 years) and males were more inclined to have high physical activity level, and experienced lower risks of OA, hypertension, and diabetes (Table 2).

Figure 2 shows the relationship between different types of physical activity and risk of OA. The three models were defined as follows: Model 1 had no covariates adjusted; Model 2 adjusted for gender and age; Model 3 further adjusted for a comprehensive set of variables including age, gender, race, level of education, BMI, smoking status, alcohol consumption, hypertension, diabetes, blood urea nitrogen, total calcium, phosphorus, triglycerides, uric acid, and total cholesterol. We found that all types of physical activity in this study were associated with OA. In Model 1, moderate work activity was a risk factor (OR: 1.20, 95% CI: 1.20–1.40), while vigorous work activity, vigorous recreational activity and walking or bicycling were protective factors. Additionally, in particular, there was the strongest statistically significant inverse relationship between vigorous recreational activity and OA risk (OR: 0.31, 95% CI: 0.21–0.48). In Model 3 after controlling for age, gender, race, education level, BMI, smoking status, alcohol consumption, hypertension, diabetes, as well as laboratory data (blood urea nitrogen, total calcium, phosphorus, triglycerides, uric acid, total cholesterol) (in the fully adjusted model) high-intensity recreational activity (OR: 0.61, 95% CI: 0.41–0.92) and moderate-intensity recreational activity (OR: 0.79, 95% CI: 0.68–0.92) were both protective factors against OA, reducing the risk by 39% and 21%, respectively. High-intensity recreational activity showed the strongest protective effect against OA.

Figure 3 illustrates that in Model 1, as the physical activity level increases, the risk of OA gradually decreases. Compared to the population who does not conduct physical activity, the risk of OA decreased by 25% (OR: 0.75, 95% CI: 0.65–0.87), 36% (OR: 0.64 95% CI: 0.54–0.76) 和32% (OR: 0.68 95% CI: 0.58–0.81) for low, medium, and high physical activity level, respectively. In Model 3, among all levels of physical activity, individuals with medium physical activity level showed the strongest protective factor against OA (OR: 0.72, 95% CI: 0.60–0.87). The dose–response relationship between total physical activity level and the risk of OA varied with age and gender. Regardless of the physical activity level, no significant correlation was found with the risk of OA in age groups of \geq 65 years (Additional file S1C). Medium physical activity, however, demonstrated preventive benefits against OA in the age groups of 20–44 years and 45–64 years and (OR:0.46, 95% CI:0.26–0.81, OR:0.73, 95% CI:0.54–0.99), reducing the risk of OA (Additional files S1A and B). In gender-stratified analyses, medium physical activity level was the strongest protective factor against OA in males (OR:0.70,95% CI:0.52–0.95), while no significant correlation was found with the risk of OA (Additional files S1A and B).

As displayed in Figs. 4A–C, across five different types of physical activity, namely vigorous work activity, vigorous recreational activity, moderate work activity, moderate recreational activity, and walking or bicycling, the impact of three physical activity levels on the risk of OA varies compared to non-physical activity. Individuals engaged in vigorous work activity with different levels of physical activity shows no significant relationship to OA risk (Fig. 4A). In addition, for vigorous recreational activity type, participating in vigorous recreational activities at a medium physical activity level reduces the incidence of OA by 59% (OR: 0.41, 95% CI: 0.17 -0.95) (Fig. 4A). In the moderate work activity type, low physical activity level is positively related to OA, raising the risk by 29%, respectively (OR:1.29, 95% CI: 1.01 -1.66). In moderate recreational activity type, a high physical activity level lowers the risk of OA by 29% (OR: 0.71, 95% CI: 0.55–0.91) (Fig. 4B). Regarding walking or bicycling related to transportation, there is no significant association between different levels of physical activity and the risk of OA (Fig. 4C).

Discussion

In this nationally representative study, vigorous recreational activities and moderate recreational activities serve as protective factors against OA, with vigorous recreational activities showing the greatest protective effect. Subdividing weekly metabolic equivalents revealed that engaging in weekly exercise at a medium physical activity level reduces the risk of OA, although this does not apply to all kinds of physical activities, including work-related activities and vigorous recreational activity. After categorizing different physical activity types, it was found that

	Physical Activity Levels (met-h/week)					
Characteristic	Q0(n=10,922) Q1(n=4775) Q2(n=3441) Q3(n=3763)				p-Value	
Age(years)						
20-44	3013(27.6)	1732(36.3)	1197(34.8)	1514(40.2)	1	
45-64	3935(36.0)	1800(37.7)	1293(37.6)	1352(35.9)	< 0.001	
≥65	3974(36.4)	1243(26.0)	951(27.6)	897(23.8)	1	
Gender						
Male	4254(38.9)	1925(40.3)	1476(42.9)	1851(49.2)	< 0.001	
Female	6668(61.1)	2850(59.7)	1965(57.1)	1912(50.8)	-	
Race						
Mexican American	1706(15.6)	629(13.2)	426(12.4)	606(16.1)	1	
Other Hispanic	1266(11.6)	450(9.4)	367(10.7)	431(11.5)	1	
Non-Hispanic white	3998(36.6)	1779(37.3)	1350(39.2)	1462(38.9)	< 0.001	
Non-Hispanic black	2651(24.3)	1139(23.9)	740(21.5)	848(22.5)	-	
Other races	1301(11.9)	778(16.3)	558(16.2)	416(11.1)	1	
Level of education						
<high school<="" td=""><td>3545(32.5)</td><td>1103(23.1)</td><td>773(22.5)</td><td>1161(30.9)</td><td>1</td></high>	3545(32.5)	1103(23.1)	773(22.5)	1161(30.9)	1	
High school	2680(24.5)	1067(22.3)	712(20.7)	978(26.0)	< 0.001	
> High school	4697(43.0)	2605(54.6)	1956(56.8)	1624(43.2)	-	
BMI status(kg/m ²)	1057 (1010)	2000(0110)	1900(00:0)	1021(1012)		
<25	2636(24.1)	1284(26.9)	1065(31.0)	1038(27.6)	< 0.001	
≥25	8286(75.9)	3491(73.1)	2376(69.0)	2725(72.4)		
Smoking status	0200(/00)		2070(0510)	2720(72.1)		
No						
Yes	6088(55.7)	2802(58.7)	2007(58.3)	1924(51.1)	< 0.001	
Alcohol consumption	0000(33.7)	2002(50.7)	2007(30.3)	1924(51.1)		
Non-drinker	1729(15.8)	643(13.5)	455(13.2)	471(12.5)	-	
<2 alcohol drinks	2266(20.7)	1152(24.1)	865(25.1)	756(20.1)	< 0.001	
≥ 2 alcohol drinks	3249(29.7)	1641(34.4)	1225(35.6)	1488(39.5)	- ~0.001	
Unspecified	3678(33.7)	1339(28.0)	896(26.0)	1438(39.3)	-	
OA	3078(33.7)	1559(28.0)	890(20.0)	1048(27.9)		
No	0412(96.2)	4265(80.3)	2121(00.7)	2207(00.2)	< 0.001	
Yes	9413(86.2)	4265(89.3)	3121(90.7)	3397(90.3)	- < 0.001	
	1509(13.8)	510(10.7)	320(9.3)	366(9.7)		
Hypertension	517((47.4))	100((20.5)	1241(20.0)	1204(24.7)	-	
NO	5176(47.4)	1886(39.5)	1341(39.0)	1304(34.7)	< 0.001	
Yes	5746(52.6)	2889(60.5)	2100(61.0)	2459(65.3)		
Diabetes	2221(20.4)	520(15.5)	464(12.5)	511(12.6)	-	
NO	2231(20.4)	738(15.5)	464(13.5)	511(13.6)	-	
Yes	8394(76.9)	3901(81.7)	2870(83.4)	3174(84.3)	< 0.001	
Unspecified	297(2.7)	136(2.8)	107(3.1)	78(2.1)	4	
Laboratory indices						
Blood urea nitrogen (mmol/L)	5.22±0.028	4.89±0.034	4.98 ± 0.041	4.86±0.039	< 0.001	
Total calcium (mmol/L)	2.34 ± 0.001	2.34 ± 0.002	2.35 ± 0.002	2.34 ± 0.002	< 0.001	
Phosphorus (mmol/L)	1.2 ± 0.002	1.2±0.003	1.2 ± 0.004	1.2 ± 0.004	< 0.001	
Triglycerides (mmol/L)	1.83 ± 0.019	1.77 ± 0.024	1.69 ± 0.029	1.71 ± 0.027	< 0.001	
Uric acid (µmol/L)	321.68 ± 1.1	319.43 ± 1.608	317.59 ± 1.966	320.49 ± 1.822	< 0.001	
Total cholesterol (mmol/L)	5.3 ± 0.021	5.29 ± 0.028	5.25 ± 0.032	5.21 ± 0.032	< 0.001	

Table 2. Baseline Characteristics of Participants by Physical Activity Levels Status: NHANES,2007–2020. n:sample size; BMI, body mass index (calculated as weight in kilograms divided by height in square meters).MET: metabolic equivalent; Continuous variables were presented by mean ± Standard error (SE), andcategorical variables were presented with numbers and percentages.

a medium physical activity level of vigorous recreational activity can reduce the risk of OA, while a high physical activity level of moderate recreational activity can lower the risk of OA. However, a low physical activity level of moderate work activity increases the risk of OA. Furthermore, the correlation between physical activity levels and the risk of OA varies with gender and age.

	activity types	Odd Ratio (95%)	P value		
Model 1					
-	s work activity				
No		ref.			
Yes		0.55 (0.37-0.81)	0.003		
	s recreational activit	•			
No		ref.			
Yes		0.31 (0.2-0.46)	< 0.001	<u> </u>	
	te work activity				
No		ref.			
Yes		1.19 (1.02-1.4)	0.027		
	te recreational activi				
No		ref.			
Yes		0.86 (0.75-1)	0.047	↓	
Walk or	bicycle				
No		ref.			
Yes		0.63 (0.52-0.77)	< 0.001	<u> </u>	
Model 2					
-	s work activity				
No		ref.			
Yes		0.86 (0.57-1.29)	0.48	••	
	s recreational activit				
No		ref.			
Yes		0.59 (0.39-0.88)	0.01	<u></u>	
	te work activity				
No		ref.			
Ves	1100	1 24 (1 05.146) 1.00-1.401	0.011	0.011	•••••••••••••••••••••••••••••••••••••••
	Moderate recreati	onal activitiy			
	No	ref.			
	Yes	0.8 (0.69-0.93)		0.003	
	Walk or bicycle				
	No	ref.			
	Yes	0.74 (0.61-0.91)		0.003	
	Model 3				
	Vigorous work act	tivity			
	No	ref.			
1	Yes	0.94 (0.62-1.42)		0.761	••••
	Vigorous recreation	onal activitiy			
	No	ref.			
	Yes	0.6 (0.4-0.91)		0.015	
	Moderate work ac	tivity			
	No	ref.			
	Yes	1.19 (1.01-1.41)		0.041	·
	Moderate recreati	onal activitiy			
	No	ref.			
	Yes	0.79 (0.68-0.92)		0.002	
	Walk or bicycle				
	No	ref.			
		0.89 (0.72-1.09)		0.25	

Fig. 2. The association between physical activity types and OA. Model 1: no covariates were adjusted; Model 2 adjusted for gender, age; Model 3 adjusted for age, gender, race, level of education, BMI, smoking status, alcohol consumption, hypertension, diabetes, blood urea nitrogen, total calcium, phosphorus, triglycerides, uric acid, total cholesterol.

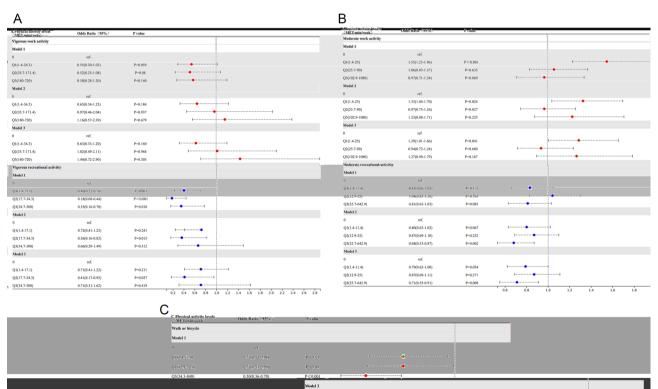
The relation between physical activity and OA has long been a focus of discussion. Physical activity, defined as movement of the body and limbs causing energy expenditure through muscle contraction, is a primary therapeutic approach against the health impacts of a sedentary lifestyle. It is also a frontline treatment for OA, with a benefit/risk ratio far exceeding that of drug therapy, supported by high levels of evidence and expert consensus, especially for lower limb OA, as confirmed by numerous studies and meta-analyses³⁰. However, in a systematic review in 2016, 18 studies, mainly small to moderate-sized quasi-experimental (non-randomized) clinical ones were identified, providing conflicting evidence on the preventive role of physical activity in knee OA following anterior cruciate ligament injury³¹. Another study demonstrated that moderate physical activity may increase the sGAG content in cartilage and potentially prevent OA. However, when sGAG content in the cartilage is depleted, exercise may induce OA³². Therefore, the type, frequency, duration, and intensity of physical activity can have different impacts on OA.

Regarding the impact of work-related activities on OA, this study found that a low physical activity level of moderate work activity increases the risk of OA, mainly due to prolonged standing, sitting, and repetitive movements in occupational activities. From a biomechanical perspective, standing places continuous compressive

.0.64(0.54-0.76)	<0.001 <0.001		
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145-1080)			* X
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(1.4-17.1)	0.84(0.72-0.98)	0.027	⊦
2(17.7-42.9)	0.69(0.58-0.83)	< 0.001	ŀ
8(45-1080)	0.88(0.73-1.05)	0.150	
odel 3			
	ref.		
(1.4-17.1)	0.86(0.74-1.01)	0.061	ŀ•
2(17.7-42.9)	0.72(0.60-0.87)	0.001	
8(45-1080)	0.93(0.78-1.12)	0.449	I
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> Fig. 3. The association between physical activity levels and OA. Model 1: no covariates were adjusted; Model 2 adjusted for age, gender; Model 3 adjusted for age, gender, race, level of education, BMI, smoking status, alcohol consumption, hypertension, diabetes, blood urea nitrogen, total calcium, phosphorus, triglycerides, uric acid, total cholesterol.



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Q2(12.9-32.1)	0.92(0.64-1.31)	P=0.632	
Q3(34.3-840)	0.81(0.56-1.15)	P=0.240	••••••••••••••••••••••••••••••••••••••
			0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3

Fig. 4. The association between physical activity levels and OA. Model 1: no covariates were adjusted; Model 2 adjusted for gender, age; Model 3 adjusted for age, gender, race, level of education, BMI, smoking status, alcohol consumption, hypertension, diabetes, blood urea nitrogen, total calcium, phosphorus, triglycerides, uric acid, total cholesterol.

loads on knee cartilage, which induces wear-promoting lubrication modes³³. Long-term engagement in occupations that involve squatting, kneeling, or climbing stairs can lead to chronic wear of joint cartilage, eventually causing OA^{34,35}. A comparative study found that the duration of squatting is positively associated with tibiofemoral OA³⁶. For individuals who sit for extended periods, prolonged sitting can lead to increased pressure within the knee joint, muscle atrophy, and joint stiffness³⁷. As muscle strength declines, joint stability is reduced, accelerating cartilage degeneration^{38,39}. On the other hand, when joints are deprived of regular loading, cartilage degradation may also occur.

In recreational activities, high physical activity levels of vigorous recreational activity and medium physical activity levels of moderate recreational activity both reduce the risk of OA. Various activities, including exercise and fitness have been validated for their protective effects against OA⁴⁰⁻⁴². Some activities, including Tai Chi⁴³, walking⁴⁴, water sports⁴⁵, and cycling⁴², stand out in both the prevention and treatment of OA. However, according to surveys, certain traumatic physical activities, including American football, soccer, weightlifting, and ice hockey, may increase the occurrence of OA⁴⁶⁻⁴⁸. Nevertheless, it is the rising rate of knee joint injuries in these groups rather than participation in physical activity itself that elevates the risk of OA.

Among different physical activity levels, a medium physical activity level has a protective effect against OA. In a study, it was found that individuals with the highest level of physical activity were characterized by an elevated risk of knee OA outcomes⁴⁹. Yang et al.⁵⁰demonstrated through histological and protein analysis that moderate-intensity treadmill exercise can improve OA by downregulating TRAIL. They also found that adaptive intensity exercise can lower the sensitivity of cartilage cells to inflammation, while excessive exercise can lead to progressive damage, hinder matrix synthesis, and stimulate the production of matrix-degrading enzymes, thereby increasing the risk of OA^{51,52}. Research has revealed that normal joint cartilage and chondrocytes can benefit from mechanical stimuli, but when the mechanical stimuli are excessive or prolonged and cannot be tolerated, it can cause damage⁴². Regular participation in physical activity has been demonstrated to be dramatically conducive to the treatment of knee OA. In addition, if patients cannot maintain activity and become sedentary, it may accelerate joint mechanical damage, potentially resulting in further deterioration of cartilage and aggravating OA⁵³. Therefore, maintaining a medium physical activity level and achieving a balance in physical activity is recommended. After conducting subgroup analyses of medium physical activity levels, this study found that the protective effect of medium physical activity levels diminished in individuals aged 65 and above. This could be due, on one hand, to the decline in joint cartilage repair capacity associated with aging⁵⁴. On the other hand, the weakening of muscles that accompanies aging makes joints more prone to damage, meaning that medium physical activity levels might no longer offer effective protection⁵⁵. Additionally, the increased likelihood of comorbidities with advancing age may further impact the effectiveness of physical activity⁵⁶.

The subgroup analysis in this study suggests that low and medium physical activity levels are protective against osteoarthritis risk in men, while no significant association was observed in women. This may be related to sex differences in joint cartilage⁵⁷. Jones et al.⁵⁸ found that men tend to have more knee cartilage compared to women. Faber et al. ⁵⁹noted that, compared to men, women have 19.9% less patellar cartilage and 46.6% less medial tibial cartilage. Additionally, Pachowsky et al.⁶⁰ discovered that women have poorer cartilage quality and lower healing capacity compared to men. Moreover, these differences could be related to metabolic variations influenced by hormone levels⁶¹.

Our study collected data from a large-scale, nationally representative sample of U.S. adults with long-term longitudinal follow-up and adjusted for most potential confounding factors. We also used appropriate NHANES sample weights to analyze the data, enhancing the reliability and generalizability of our results. The results indicated that vigorous recreational activity and moderate recreational activity are protective factors against OA. Specifically, at a medium physical activity level, vigorous recreational activity can reduce the risk of OA, while at a high physical activity level, moderate recreational activity can also reduce the risk. However, moderate work activity at a low physical activity level is associated with an increased risk of OA. Based on these findings, we can develop targeted exercise recommendations for individuals at higher risk of OA, guide individual physical activity interventions, and improve public health strategies to reduce the incidence of OA. Finally, multiple subgroup analyses were performed to confirm the robustness of the results.

Despite these strengths, our study has certain limitations. Firstly, it is a cross-sectional study, and NHANES data are typically cross-sectional, providing health and nutrition information at a specific point in time without revealing trends or causal relationships. Secondly, This study relied on self-reported data to determine the presence of OA, which may introduce reporting bias and result in some individuals with actual OA being incorrectly classified as non-OA. This could lead to an underestimation of the true prevalence of OA and potentially impact the statistical analysis results. However, despite the possibility of misclassification of OA cases, the large sample size used in this study enhances the generalizability of the findings. Additionally, the use of multiple models and subgroup analyses to adjust for confounding factors increases the reliability of the results. Therefore, the findings of this study still maintain a certain degree of validity and robustness. Thirdly, despite adjusting for various covariates, some potential confounding factors might still have been overlooked.

Conclusion

To conclude, this study demonstrates the cross-sectional impact of physical activity on OA. Among all types of physical activity, vigorous recreational activity and moderate recreational activity are found to have a preventive effect on OA. In terms of physical activity levels, low physical activity levels of moderate work activity are associated with an increased risk of OA, while moderate physical activity levels are confirmed to have a protective effect against OA in the age groups of 20–44 and 45–64. However, gender-stratified analyses reveal that both low and moderate physical activity levels provide protection against OA in males, with moderate physical activity levels showing a more significant protective effect.

Data availability

The datasets generated and analysed during the current study are available in the National Health and Nutrition Examination Survey repository, https://www.cdc.gov/nchs/nhanes/index.htm.

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References

- 1. Woolf, A. D. & Pfleger, B. Burden of major musculoskeletal conditions. Bull World Health Organ 81, 646-656 (2003).
- 2. Glyn-Jones, S. et al. Osteoarthritis. Lancet 386, 376-387 (2015).
- 3. Katz, J. N., Arant, K. R. & Loeser, R. F. Diagnosis and treatment of hip and knee osteoarthritis: A review. JAMA 325, 568-578 (2021).
- Recreational Physical Activity and Risk of Incident Knee Osteoarthritis: An International Meta-Analysis of Individual Participant– Level Data - Gates - 2022 - Arthritis & Rheumatology - Wiley Online Library. https://acrjournals.onlinelibrary.wiley.com/ doi/https://doi.org/10.1002/art.42001.
- 5. Verweij, L. M., van Schoor, N. M., Dekker, J. & Visser, M. Distinguishing four components underlying physical activity: a new approach to using physical activity questionnaire data in old age. *BMC Geriatrics* **10**, 20 (2010).
- 6. Wu, Y. et al. Weight-bearing physical activity, lower-limb muscle mass, and risk of knee osteoarthritis. JAMA Netw Open 7, e248968 (2024).
- Gay, C., Chabaud, A., Guilley, E. & Coudeyre, E. Educating patients about the benefits of physical activity and exercise for their hip and knee osteoarthritis Systematic literature review. Ann. Phys. Rehabil. Med. 59, 174–183 (2016).
- 8. Kraus, V. B. *et al.* Effects of physical activity in knee and hip osteoarthritis: A systematic umbrella review. *Med. Sci. Sports Exerc.* **51**, 1324–1339 (2019).
- Timmins, K. A., Leech, R. D., Batt, M. E. & Edwards, K. L. Running and knee osteoarthritis: A systematic review and meta-analysis. *Am. J. Sports Med.* 45, 1447–1457 (2017).
- 10. Racunica, T. L. *et al.* Effect of physical activity on articular knee joint structures in community-based adults. *Arthritis Rheum.* 57, 1261–1268 (2007).
- Perez-Lasierra, J. L., Casajus, J. A., González-Agüero, A. & Moreno-Franco, B. Association of physical activity levels and prevalence of major degenerative diseases: Evidence from the national health and nutrition examination survey (NHANES) 1999–2018. *Exp. Gerontol.* 158, 111656 (2022).
- 12. Migliorini, F., Torsiello, E., La Padula, G., Oliva, F. & Maffulli, N. The association between sex and osteoarthritis in the physically active population: A systematic review. *Sports Med. Arthrosc. Rev.* **30**, 87–91 (2022).
- van der Wilk, S. et al. Physical activity after revision knee arthroplasty including return to sport and work: a systematic review and meta-analysis including GRADE. BMC Musculoskelet. Disord. 24, 368 (2023).
- 14. Bassi, J. S., Chan, J. P., Johnston, T. & Wang, D. Return to work and sport after distal femoral osteotomy: A systematic review. Sports Health 14, 681–686 (2022).
- 15. Keating, X. D. *et al.* Reliability and concurrent validity of global physical activity questionnaire (GPAQ): A systematic review. *Int. J. Environ. Res. Public Health* **16**, 4128 (2019).
- 16. Kunene, S. H. & Taukobong, N. P. Level of physical activity of health professionals in a district hospital in KwaZulu-Natal South Africa. *S Afr. J. Physiother* **71**, 234 (2015).
- 17. Chen, L. *et al.* Risk/benefit tradeoff of habitual physical activity and air pollution on chronic pulmonary obstructive disease: findings from a large prospective cohort study. *BMC Med* **20**, 70 (2022).
- Li, C., Shang, S. & Liang, W. Physical activity types, physical activity levels and risk of diabetes in general adults: The NHANES 2007–2018. Int. J. Environ. Res. Public Health 20, 1398 (2023).
- 19. Sönmez, E. et al. Hyperthyroidism influences renal function. Endocrine 65, 144-148 (2019).
- Alhassan, E., Nguyen, K., Hochberg, M. C. & Mitchell, B. D. Causal factors for osteoarthritis: A scoping review of mendelian randomization studies. *Arthritis Care Res (Hoboken)* https://doi.org/10.1002/acr.25252 (2023).
- Apurba, G. & Sudip, B. Biomonitoring the skeletal muscle metabolic dysfunction in knee osteoarthritis in older adults: Is Jumpstart Nutrition^{*} Supplementation effective?. Caspian J. Intern. Med. 14, 590–606 (2023).
- 22. Jiang, H. *et al.* Adiponectin, may be a potential protective factor for obesity-related osteoarthritis. *Diabetes Metab. Syndr. Obes.* 15, 1305–1319 (2022).
- Xiao, L., Lin, S. & Zhan, F. The association between serum uric acid level and changes of MRI findings in knee osteoarthritis: A retrospective study (A STROBE-compliant article). *Medicine (Baltimore)* 98, e15819 (2019).
- Siddiq, M. A. B., Jahan, I. & Rasker, J. J. Statin in clinical and preclinical knee osteoarthritis-what e vidence exists for future clinical use?-A literature review. Curr. Rheumatol Rev. 19, 270–280 (2023).
- Felson, D. T. & Zhang, Y. Smoking and osteoarthritis: a review of the evidence and its implications. Osteoarthr. Cartil. 23, 331–333 (2015).
- To, K. et al. The association between alcohol consumption and osteoarthritis: A meta-analysis and meta-regression of observational studies. Rheumatol. Int. 41, 1577–1591 (2021).
- 27. Veronese, N. et al. Knee osteoarthritis and risk of hypertension: A longitudinal cohort study. Rejuvenation Res. 21, 15-21 (2018).
- Schwarz, S., Mrosewski, I., Silawal, S. & Schulze-Tanzil, G. The interrelation of osteoarthritis and diabetes mellitus: considering the potential role of interleukin-10 and in vitro models for further analysis. *Inflamm. Res.* 67, 285–300 (2018).
- 29. Hsu, J. Y. & Small, D. S. Calibrating sensitivity analyses to observed covariates in observational studies. *Biometrics* 69, 803-811 (2013).
- 30. Daste, C. et al. Physical activity for osteoarthritis: Efficiency and review of recommandations. Joint Bone Spine 88, 105207 (2021).
- A systematic review to evaluate exercise for anterior cruciate ligament injuries: does this approach reduce the incidence of knee osteoarthritis? - PubMed. https://pubmed.ncbi.nlm.nih.gov/27843365/.
- 32. Siebelt, M. *et al.* Increased physical activity severely induces osteoarthritic changes in knee joints with papain induced sulfateglycosaminoglycan depleted cartilage. *Arthritis. Res. Ther.* **16**, R32 (2014).
- Miller, R. H., Brent Edwards, W. & Deluzio, K. J. Energy expended and knee joint load accumulated when walking, running, or standing for the same amount of time. *Gait Posture* 41, 326–328 (2015).
- 34. Occupational risk factors for osteoarthritis of the knee: a meta-analysis PubMed. https://pubmed.ncbi.nlm.nih.gov/21382500/.
- Ezzat, A. M., Cibere, J., Koehoorn, M. & Li, L. C. Association between cumulative joint loading from occupational activities and knee osteoarthritis. Arthritis Care Res. (Hoboken) 65, 1634–1642 (2013).
- Zhang, Y. et al. Association of squatting with increased prevalence of radiographic tibiofemoral knee osteoarthritis: The Beijing osteoarthritis study. Arthritis Rheum. 50, 1187–1192 (2004).
- Lee, J. et al. Sedentary behavior and physical function: Objective evidence from the osteoarthritis initiative. Arthritis Care Res. (Hoboken) 67, 366–373 (2015).

- 38. Xu, J. *et al.* Knee muscle atrophy is a risk factor for development of knee osteoarthritis in a rat model. J. Orthop. Translat. 22, 67–72 (2020).
- 39. Peng, P. et al. Association between sarcopenia and osteoarthritis among the US adults: A cross-sectional study. Sci. Rep. 14, 296 (2024).
- 40. Exercise Therapy for Knee Osteoarthritis: A Systematic Review and Network Meta-analysis PubMed. https://pubmed.ncbi.nlm. nih.gov/37346776/.
- 41. Nagao, M. et al. Physical activity for knee osteoarthritis. Clin. Calcium 27, 25-30 (2017).
- 42. Jia, S., Yu, Z. & Bai, L. Exerkines and osteoarthritis. Front. Physiol. 14, 1302769 (2023).
- 43. Zhuang, S.-Z., Chen, P.-J., Han, J. & Xiao, W.-H. Beneficial effects and potential mechanisms of Tai Chi on lower limb osteoarthritis: A biopsychosocial perspective. *Chin. J. Integr. Med.* **29**, 368–376 (2023).
- Core and adjunctive interventions for osteoarthritis: efficacy and models for implementation PubMed. https://pubmed.ncbi.nlm. nih.gov/32661322/.
- 45. Aquatic exercise for the treatment of knee and hip osteoarthritis PubMed. https://pubmed.ncbi.nlm.nih.gov/27007113/.
- 46. Early-onset arthritis in retired National Football League players PubMed. https://pubmed.ncbi.nlm.nih.gov/19953841/
- 47. Kujala, U. M. *et al.* Knee osteoarthritis in former runners, soccer players, weight lifters, and shooters. *Arthritis Rheum.* **38**, 539–546 (1995).
- Knee injuries account for the sports-related increased risk of knee osteoarthritis PubMed. https://pubmed.ncbi.nlm.nih.gov/ 16978252/.
- Meeting physical activity guidelines and the risk of incident knee osteoarthritis: a population-based prospective cohort study -PubMed. https://pubmed.ncbi.nlm.nih.gov/23983187/.
- Moderate Mechanical Stimulation Protects Rats against Osteoarthritis through the Regulation of TRAIL via the NF- κ B/NLRP3 Pathway - PubMed. https://pubmed.ncbi.nlm.nih.gov/32566090/.
- Mechanical stress protects against osteoarthritis via regulation of the AMPK/NF-κB signaling pathway PubMed. https://pubmed. ncbi.nlm.nih.gov/30311192/.
- 52. Liu, J. et al. Exercise induced meteorin-like protects chondrocytes against inflammation and pyroptosis in osteoarthritis by inhibiting PI3K/Akt/NF-κB and NLRP3/caspase-1/GSDMD signaling. Biomed Pharmacother 158, 114118 (2023).
- Changes of articular cartilage after immobilization in a rat knee contracture model PubMed. https://pubmed.ncbi.nlm.nih.gov/ 18683886/.
- Ding, C., Cicuttini, F., Scott, F., Cooley, H. & Jones, G. Association between age and knee structural change: a cross sectional MRI based study. Ann. Rheum. Dis. 64, 549–555 (2005).
- 55. Yang, J., Jiang, T., Xu, G., Wang, S. & Liu, W. Exploring molecular mechanisms underlying the pathophysiological association between knee osteoarthritis and sarcopenia. *Osteoporos Sarcopenia* **9**, 99–111 (2023).
- Liu, Y. & Du, G. Blood pressure is associated with knee pain severity in middle-aged and elderly individuals with or at risks for osteoarthritis: Data from the Osteoarthritis Initiative. BMC Musculoskelet. Disord. 25, 536 (2024).
- 57. O'Connor, M. I. Sex differences in osteoarthritis of the hip and knee. JAAOS J. Am. Acad. Orthop. Surg. 15, S22 (2007).
- Sex and site differences in cartilage development: a possible explanation for variations in knee osteoarthritis in later life PubMed. https://pubmed.ncbi.nlm.nih.gov/11083279/.
- 59. Faber, S. C. *et al.* Gender differences in knee joint cartilage thickness, volume and articular surface areas: assessment with quantitative three-dimensional MR imaging. *Skeletal Radiol.* **30**, 144–150 (2001).
- Pachowsky, M. L. et al. 3D-isotropic high-resolution morphological imaging and quantitative T2 mapping as biomarkers for gender related differences after matrix-associated autologous chondrocyte transplantation (MACT). J. Orthop. Res. 32, 1341–1348 (2014).
- 61. Amesbury, R. *et al.* Gender differences in patterns of cartilage loss: Data from the Osteoarthritis Initiative. *Osteoarthr. Cartil.* **32**, 1149 (2024).

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Author contributions

Formal analysis, C.H and Z.G.; Funding acquisition, E.G. and L.D.; Z.F. and J.X. prepared Figs. 1, 2, 3 and 4; Z.P. and W.L. prepared additional files 1, 2 All authors have read and agreed to the published version of the manuscript.

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Competing interests

The authors declare no competing interests.

Ethical approval

Ethics approval Informed consent was given by participants prior to performing NHANES and ethics approval was obtained from the Research Ethics Review Board at the National Centre for Health Statistics, https://www.cdc.gov/nchs/nhanes/irba98.htm

Additional information

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