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ORIGINAL ARTICLE

Physical activity, long-term fine particulate matter exposure and type 2 diabetes incidence: A prospective cohort study

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Abstract

Background: Despite the adverse effects of ambient fine particulate matter ($PM_{2.5}$) on type 2 diabetes and the beneficial role of physical activity (PA), the influence of $PM_{2.5}$ on the relationship between PA and type 2 diabetes remains unclear.

Methods: In this prospective study with 71,689 participants, PA was assessed by a questionnaire and was categorized into quartiles for volume and three groups for intensity. Long-term $PM_{2.5}$ exposure was calculated using 1-km resolution satellite-based $PM_{2.5}$ estimates. $PM_{2.5}$ exposure and PA's effect on type 2 diabetes were assessed by cohort-stratified Cox proportional hazards models, individually and in combination.

Results: In 488,166 person-years of follow-up, 5487 incident type 2 diabetes cases were observed. The association between PA and type 2 diabetes was modified by $PM_{2.5}$. Compared with the lowest quartile of PA volume, the highest quartile was associated with reduced type 2 diabetes risk in low $PM_{2.5}$ stratification (≤65.02 μg/m^3) other than in high $PM_{2.5}$ stratification (>65.02 μg/m^3), with the hazard ratio (HR) of 0.75 (95% confidence interval [CI]: 0.66–0.85) and 1.10 (95% CI: 0.99–1.22), respectively. Similar results were observed for PA intensity. High $PM_{2.5}$ exposure combined with the highest PA

levels increased the risk of type 2 diabetes the most (HR = 1.79, 95% CI: 1.59–2.01 for PA volume; HR = 1.82, 95% CI: 1.64–2.02 for PA intensity).
Conclusion: PA could reduce type 2 diabetes risk in low-pollution areas, but high $PM_{2.5}$ exposure may weaken or even reverse the protective effects of PA. Safety and health benefits of PA should be thoroughly assessed for long-term polluted residents.

KEYWORDS
fine particulate matter, physical activity, type 2 diabetes

Key points

- $PM_{2.5}$ modifies the association between physical activity (PA) and type 2 diabetes.
- PA reduces type 2 diabetes risk at lower $PM_{2.5}$ stratum but increase at higher strata.
- The benefits of PA are weakened by the detrimental effects of $PM_{2.5}$ exposure.
- Call for consideration of the joint impact of PA and air pollution on health.

1 | INTRODUCTION

The prevalence and mortality of type 2 diabetes rise rapidly, which has evolved into a pressing global public health concern, with a tremendous burden worldwide increasing from 4.9 million disability-adjusted life years (DALYs) in 2010 to 6.6 million in 2019.[1,2] China has become a country with one of the highest type 2 diabetes prevalence rates in the world, which has risen from less than 1% in 1980[3] to 12.4% in 2018,[4] and the prevalence of prediabetes at 38.1% in 2018 poses a high risk for future diabetes development. Hence, China was confronted with a severe challenge in controlling type 2 diabetes.

Previous literature has confirmed that adherence to physical activity (PA) can lead to a range of beneficial health effects, for example, PA may link to a decreased risk of diabetes.[5–8] The American Diabetes Association (ADA) ardently advocated regular PA as a paramount strategy for the prevention and management of type 2 diabetes.[7] However, particularly in heavily polluted regions, increased PA may simultaneously elevate inhaled concentrations of ambient fine particulate matter ($PM_{2.5}$), potentially intensifying the adverse health consequences of atmospheric pollutants. Previous epidemiological studies have shown inconsistency in the relationship between PA and the risk of type 2 diabetes across different $PM_{2.5}$ levels.[9–12] Researchers in South Korea discovered that even at high $PM_{2.5}$ levels ($\geq 27.88\ \mu g/m^3$), groups who engaged in moderate-to-vigorous physical activity (MVPA) 1–2, 3–4, and at least five times per week could minimize the risk of type 2 diabetes.[10] Similar findings from the UK Biobank indicated that there was no significant difference between PA and the risk of type 2 diabetes at different $PM_{2.5}$ levels.[11,12] These insignificant differences between PA and risk of type 2 diabetes across various $PM_{2.5}$ levels might be related to the relatively low $PM_{2.5}$ concentrations (all less than $30\ \mu g/m^3$).

To data, only a cross-sectional study conducted in southwestern China observed that severe pollution ($PM_{2.5} \geq 61\ \mu g/m^3$) may increase the risk of type 2 diabetes, even surpassing the protective effects of PA.[9] Nevertheless, few high-quality, prospective multicenter studies have comprehensively interpreted the relationship between PA and type 2 diabetes investigating a range of $PM_{2.5}$ concentrations, which is crucial in guiding the public to engage in appropriate PA to prevent type 2 diabetes in China or other low- and middle-income countries (LMICs). Besides, previous studies primarily focused on the effect of volume, frequency, and types of PA on type 2 diabetes,[13] while few studies contain an additional dimension of evaluating PA intensity.

The primary objective of this study was to assess the influence of long-term exposure to $PM_{2.5}$ on the association between regular PA and the risk of type 2 diabetes. We utilized data from the Prediction for Atherosclerotic Cardiovascular Disease Risk in China (China-PAR) project,[14,15] a nationwide population-based prospective cohort study, in combination with high-resolution satellite-based $PM_{2.5}$ exposure.

2 | METHODS

2.1 | Study population

The study participants were drawn from the China-PAR project with three subcohorts, including China Multi-Center Collaborative Study of Cardiovascular Epidemiology (China MUCA 1998), International

Collaborative Study of Cardiovascular Disease in Asia (InterASIA), and Community Intervention of Metabolic Syndrome in China and Chinese Family Health Study (CIMIC). The design of this cohort has already been thoroughly explained in previous publications.[14,15] In brief, the baseline survey of the China MUCA 1998 commenced in 1998, employing a cluster random sampling method to select participants aged 35–59 years from 15 clusters across China. InterASIA was initiated during 2000–2001, with a stratified four-stage sampling approach based on geographical regions (Northern and Southern China, divided by the Yangtze River) and urbanization levels (urban and rural) to obtain a nationally representative sample. CIMIC started in 2007–2008 and recruited participants aged 18 years and older through cluster random sampling at four survey sites in central and eastern China. InterASIA and China MUCA 1998 both followed up during 2007–2008. Subsequently, all subcohorts followed up between 2012 and 2015. Data collection was conducted after obtaining written informed consent from the participants. The China-PAR project received approval from the Ethics Committee of Fuwai Hospital in Beijing, China, and the ethical approval number was 2012-399.

Initially, a total of 113,448 participants aged ≥18 years were enrolled at the baseline. Since $PM_{2.5}$ exposure data had not been available until 2000, the baseline for this study was set at the year 2000. After the exclusion of 8313 participants due to loss to follow-up, we obtained 105,135 study subjects with follow-up information available. Of the participants, 11,232 were excluded because they either died or were diagnosed with type 2 diabetes or had missing information on their diabetes status at baseline or before 2000. Further exclusions involved 85 with incomplete residence data, 2307 missing PA information at baseline, and 19,822 missing diabetes-related information at follow-up, leaving 71,689 participants for the final analysis (Supporting Information S1: Figure 1).

2.2 | Data collection

The local community clinics or health stations served as the examination sites for collecting baseline data. Trained staff members presented a standardized questionnaire to the participants to gather data on residential addresses, sociodemographic characteristics, family history, and personal medical history, as well as lifestyle risk factors (smoking, alcohol consumption, and PA). Smokers were defined as individuals who had either consumed a minimum of 400 cigarettes or 500 g of tobacco throughout their lifetime or had smoked at least one cigarette daily for over a year. Current smokers were those who still smoked during the survey. There were three categories for smoking status: never smoked, former smoker, and current smoker. Alcohol drinking was defined by whether individuals had consumed alcohol at least once a week in the year before. The education level is separated into two categories based on whether or not they have attended high school or above (≥10 years). Systolic/diastolic blood pressure readings of 140/90 mmHg or usage of antihypertensive drugs during the previous 2 weeks were considered hypertension. The measurement of blood pressure was performed by trained medical professionals based on the protocol recommended by the American Heart Association.[16] Participants' blood pressure was taken on the right upper arm every 30 s for three times in the sitting posture after a 5-min rest period. The blood pressure for each participant was calculated by taking the average of three readings. A family history of type 2 diabetes was considered positive if a parent or sibling had type 2 diabetes. The participants, dressed in light clothing and barefoot, underwent standardized height and weight measurements. Body mass index (BMI) was calculated as body weight (kg) divided by squared height (m^2). After 10 or more hours of overnight fasting, the collected blood samples were stored at Fuwai Hospital of the Chinese Academy of Medical Sciences. Detailed information regarding the measurement of blood samples was provided in Supporting Information method. Serum glucose was measured by a modified hexokinase enzymatic method (Hitachi automatic clinical analyzer, model 7060; Hitachi), and lipid concentrations (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C]) were enzymatically using commercially available reagents. Dyslipidemia was defined as participants having TC ≥ 240 mg/dL, or triglycerides ≥200 mg/dL, or low-density lipoprotein cholesterol (LDL-C) ≥ 160 mg/dL, or HDL-C < 40 mg/dL, or those who had started lipid-lowering medication in the previous 2 weeks.

2.3 | Ascertainment of outcomes

Type 2 diabetes was defined by a fasting plasma glucose level of ≥126 mg/dL or use of insulin or oral hypoglycemic agents.[17] We identified subjects who developed type 2 diabetes during the follow-up (from 2000 to 2015) by this criterion. The event date of type 2 diabetes was defined as the date of first diagnosis or first use of insulin or oral hypoglycemic agents.

2.4 | Exposure assessment

From 2000 to 2015, we evaluated long-term $PM_{2.5}$ exposure for each participant utilizing satellite-based $PM_{2.5}$ data at 1-km spatial resolution, and the corresponding assessment methodology article has been published.[18] Briefly, utilizing high-resolution satellite aerosol optical depth (AOD) data from the National Aeronautics and Space Administration

(NASA) Aqua and Terra satellites, along with land-use, road, meteorological, and population-density data, the spatiotemporal model estimated $PM_{2.5}$ exposure throughout China from 2000 to 2015 at a spatial resolution of 1×1 km. Validation of the model for $PM_{2.5}$ predictions using national air quality monitoring data from the Ministry of Ecology and Environment (MOE) provided a 10-fold cross-validation R^2 of 0.93, indicating a high degree of accuracy.[18] To assess the precision in forecasting historical $PM_{2.5}$ concentrations (earlier than 2013), a comparative analysis was performed by contrasting the model predictions with monitoring data derived from Hong Kong, Taiwan, and the US Embassy in Beijing, Shanghai, and Guangzhou. At the annual level, our model achieved an R^2 value of 0.80 and a root mean squared error of 8.90 μg/m^3. Subsequently, the latitude and longitude corresponding to the dwelling addresses were matched with $PM_{2.5}$ concentration. Considering changes in residential history, we assigned weights based on residency duration and calculated time-weighted average $PM_{2.5}$ concentration for each participant from 2000 to 2015. The spatial distribution of average $PM_{2.5}$ concentrations in China (from 2000 to 2015) and labeling of provinces and cities in the China-PAR project (2000–2015) has been published elsewhere.[19] Participants were split into two categories based on their median $PM_{2.5}$ exposure: low (≤65.02 μg/m^3) and high (>65.02 μg/m^3).

2.5 | PA evaluations

The information of PA for the China MUCA 1998, InterASIA, and CIMIC encompassed four aspects: occupation, housework, transportation, and leisure time. The InterASIA and CIMIC inquired about the amount of time spent on engaging in high-intensity PA (such as running, weightlifting, etc.), moderate-intensity PA (such as walking, dancing, etc.), low-intensity PA (such as walking, cooking, etc.), other sedentary activities, and sleeping on workdays and weekends in the previous year. The China MUCA 1998 investigated the amount of time spent on more specific types of PA (such as riding a motorcycle, walking, etc.) at workdays and weekends during the past year. Metabolic equivalent (MET) served as a measure of PA intensity. One MET was equivalent to the energy expenditure of 1 kilocalorie per kilogram of body weight per hour. The low-, moderate-, and high-intensity of PA in daily work and after work were assigned 2, 4, and 8 METs, respectively. The MET assignment for the specific types of PA was calculated using the 2024 Physical Activity Summary.[20] PA volume (MET-h/d) was equal to the MET value in each PA category multiplied by the time spent in that kind of PA. The average PA intensity is equivalent to PA volume split by total daily hours on PA.[21] The individuals were grouped by the quartiles (Q) of PA volume: Q1 (≤16.0 MET-h/d), Q2 (>16.0–31.0 MET-h/d), Q3 (>31.0–52.0 MET-h/d), and Q4 (>52.0 MET-h/d). Average PA intensity was used to classify participants as light intensity (1.6–<3.0 MET), moderate intensity (3.0–<6.0 MET), or vigorous intensity (≥6.0 MET).

2.6 | Statistical analysis

The person-years of follow-up was calculated from the date of recruitment or January 1, 2000 (if the date of recruitment was before 2000) to the date of the type 2 diabetes onset, death, or loss to follow-up (which occurred first). Continuous variable descriptive statistics are reported as mean (standard deviations [SDs]), while categorical variable descriptive statistics are presented as percentages. A linear regression model and Mantel-Haenszel χ^2 test were used to test for trends between groups of continuous variables and categorical variables, relatively.

Cohort-stratified Cox proportional hazards regression models were used to estimate the hazard ratio (HR) and 95% confidence intervals (95% CIs) for risk of type 2 diabetes in relation to $PM_{2.5}$ exposure levels (per 10 μg/m^3 for continuous variable; the low exposure as a reference for categorical variable), PA volume, and average PA intensity, with the duration of follow-up as a time scale. Schoenfeld residuals were used to evaluate the proportional hazard assumptions, and no violations were found. To account for potential confounders, we identified the minimal sufficient set of covariates for adjustment using directed acyclic graph (Supporting Information S1: Figure 2).[22] We additionally adjusted for baseline blood glucose level and BMI based on previous literature.[23,24] We established three models: model 1 was a crude model including age and sex; model 2 added urbanization (urban or rural), geographical region (north, east, northeastern, south, central, southwestern, and northwestern), education level (≥10 years or not), smoking status (never, former, or current), alcohol drinking (yes or no), and family history of type 2 diabetes (yes or no). Model 3 expanded on model 2 by plus BMI, baseline blood glucose level, and $PM_{2.5}$ exposure (for the association with PA volume or average PA intensity) or PA volume (for the association with $PM_{2.5}$ exposure).

Additionally, stratified analyses were conducted to explore the association between PA volume (or average PA intensity) and the risk of type 2 diabetes under varying levels of $PM_{2.5}$ exposure. To identify potential trends of PA in each $PM_{2.5}$ stratification, the median values of each PA category were treated as continuous variables across three models. The fully adjusted model utilized restricted cubic splines (RCS) with three knots, chosen based on the Akaike information criterion (AIC), to graphically illustrate the dose–response relationships between PA volume (or average PA intensity) and the risk of type 2 diabetes, stratified by $PM_{2.5}$ exposure.[25] The reference group, composed of individuals with low $PM_{2.5}$ exposure and the lowest PA volume (or average PA intensity), was used to evaluate the combined effects of $PM_{2.5}$ exposure and

PA, with HRs for incident type 2 diabetes estimated for 8 (or 6) subgroups within model 3. The bivariate response surface was used to visually depict the combined influence of $PM_{2.5}$ exposure and PA volume (or average PA intensity). We also explored possible interactions between PA and $PM_{2.5}$ exposure using likelihood ratio tests in model 3 with and without the interaction term of $PM_{2.5}$ and PA volume (or average PA intensity).

To verify the robustness of our findings, we performed several sensitivity analyses: (1) excluding the individuals who occurred type 2 diabetes during the first follow-up year; (2) replacing average $PM_{2.5}$ exposure from 2000 to 2015 with average $PM_{2.5}$ exposure in the 3/5 years before the onset of type 2 diabetes; (3) using time-varying Cox proportional hazard models on time scales of 1 years to mitigate potential exposure misclassification due to the development of type 2 diabetes before 2015; (4) replacing average $PM_{2.5}$ exposure from 2000 to 2015 with $PM_{2.5}$ exposure at baseline 2000 to ensure consistency between the $PM_{2.5}$ exposure and the PA exposure time periods; (5) substituting the amount of alcohol consumed for alcohol drinking in the model 3; (6) excluding people with type 2 diabetes defined by the use of insulin or oral hypoglycemic agents; (7) incorporating self-reported diabetes diagnoses into the original definition of outcomes; (8) Fine-Gray competing risk regression model substituting Cox proportional hazards regression models. All sensitivity analyses were conducted with stratified analyses and interaction effect.

Statistical tests were conducted with two-sided significance, defined as $p < 0.05$. All analyses and plots were performed in SAS 9.4 (SAS Institute Inc.) and R software (version 4.2.2), respectively.

3 | RESULTS

3.1 | Baseline characteristics of participants

Descriptive statistics of baseline characteristics for 71,689 participants by PA volume was demonstrated in Table 1. During a median follow-up of 5.93 years,

TABLE 1 Baseline characteristics based on PA volume quartiles.

	PA volume (MET-h/d)					
Characteristics	**Overall**	**Q1 (≤16.0)**	**Q2 (>16.0–31.0)**	**Q3 (>31.0–52.0)**	**Q4 (>52.0)**	***p* value**
No. of participants	71,689	19,825	16,061	18,605	17,198	
Age, mean (SD), years	51.28 (11.74)	53.82 (12.92)	49.68 (11.80)	50.09 (11.11)	51.13 (10.35)	<0.001
Male, *N* (%)	28,365 (39.57)	7474 (37.70)	5618 (34.98)	7479 (40.20)	7794 (45.32)	<0.001
Urban, *N* (%)	7022 (9.80)	3771 (19.02)	2618 (16.30)	537 (2.89)	96 (0.56)	<0.001
Education (≥10 years), *N* (%)	9599 (13.43)	3819 (19.39)	3062 (19.11)	1631 (8.78)	1087 (6.33)	<0.001
BMI, mean (SD), kg/m^2	23.83 (3.57)	24.11 (3.66)	23.72 (3.53)	23.76 (3.52)	23.70 (3.55)	<0.001
Smoking status, *N* (%)						<0.001
Never	53,282 (74.60)	15,118 (76.54)	12,106 (75.89)	13,723 (74.01)	12,335 (71.84)	
Former	2568 (3.60)	863 (4.37)	607 (3.80)	563 (3.04)	535 (3.12)	
Current	15,569 (21.80)	3771 (19.09)	3240 (20.31)	4257 (22.96)	4301 (25.05)	
Alcohol drinking, *N* (%)	12,685 (17.70)	3067 (15.48)	2506 (15.60)	3414 (18.35)	3698 (21.50)	<0.001
Family history of type 2 diabetes, *N* (%)	2461 (3.43)	769 (3.88)	709 (4.41)	565 (3.04)	418 (2.43)	<0.001
Baseline blood glucose level, mean (SD), mg/dL	87.87 (13.76)	89.10 (13.49)	89.22 (13.16)	87.27 (13.85)	85.81 (14.22)	0.104
SBP, mean (SD), mmHg	128.82 (21.35)	131.96 (23.31)	126.85 (20.68)	127.77 (20.21)	128.18 (20.38)	<0.001
DBP, mean (SD), mmHg	79.47 (11.65)	80.62 (11.82)	79.05 (11.36)	79.06 (11.60)	78.99 (11.70)	0.578
Dyslipidemia, *N* (%)	21,464 (29.96)	6532 (32.97)	5052 (31.47)	5376 (28.91)	4504 (26.20)	<0.001
$PM_{2.5}$ exposure, mean (SD), $\mu g/m^3$	67.74 (13.76)	69.25 (14.35)	65.65 (13.02)	66.94 (13.06)	68.81 (14.15)	<0.001
PA volume, mean (SD), MET-h/d	35.05 (23.15)	10.05 (5.19)	22.91 (3.75)	40.99 (6.41)	68.77 (10.55)	<0.001
PA intensity, mean (SD), MET	4.13 (2.06)	2.28 (0.83)	2.87 (1.16)	4.69 (1.44)	6.67 (1.11)	<0.001

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; MET, metabolic equivalent; MET-h/d, MET-hours/day; PA, physical activity; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; Q, quartile; SBP, systolic blood pressure; SD, standard deviations.

we observed 5487 incident cases of type 2 diabetes with a cumulative incidence of 7.65%. The mean age at baseline of study participants was 51.28 (11.74) years, and 39.57% of them were male. Participants in the first quartile of PA volume were the youngest. And participants with higher PA volume tended to be male, smokers, and drinkers, with lower BMI, blood glucose level, and education level, but displayed a greater level of PA intensity. Moreover, the average $PM_{2.5}$ concentrations from 2000 to 2015 varied from 31.17–88.84 μg/m^3. Participants exposed to higher concentrations of $PM_{2.5}$ were prone to have a higher level of PA intensity, BMI, and blood glucose. The baseline characteristics of the subgroups based on PA intensity were shown in Supporting Information S1: Table 1. And the baseline characteristics with different PA levels under $PM_{2.5}$ stratification were shown in Supporting Information Tables 2 and 3. Participants excluded from the current analysis tended to be younger, have lower BMI, and were more likely to be men, smokers, and drinkers (Supporting Information S1: Table 4).

3.2 | Associations of $PM_{2.5}$ exposure or PA with type 2 diabetes

We estimated the independent relationships between prolonged exposure to $PM_{2.5}$ as well as PA and the development of type 2 diabetes (Table 2). In the fully adjusted model, long-term exposure to $PM_{2.5}$ was significantly associated with a heightened risk of type 2 diabetes, and each 10 μg/m^3 increment of $PM_{2.5}$ was associated with a 29% (HR = 1.32, 95% CI: 1.29–1.36) increased risk of type 2 diabetes. High $PM_{2.5}$ exposure was associated with a 98% (HR = 1.98, 95% CI: 1.85–2.13) increased risk of type 2 diabetes in model 3. In contrast, an inverse association between PA and the risk of type 2 diabetes was clearly observed. Compared to the lowest quartile of PA volume (≤16.0 MET-h/d), the second to fourth quartiles showed fully adjusted HRs of 0.90 (95% CI: 0.83–0.96), 0.84 (95% CI: 0.78–0.91), and 0.90 (95% CI: 0.83–0.97), respectively (P_{trend} = 0.011). Similar results were presented in PA intensity; the fully adjusted HRs of moderate intensity and vigorous intensity were 0.81 (95% CI: 0.76–0.87) and 0.85 (95% CI: 0.79–0.92), respectively (P_{trend} = 0.091).

TABLE 2 HRs and 95% CI for type 2 diabetes associated with long-term $PM_{2.5}$ exposure, as well as volume and intensity of PA.

Index	No. of cases	Person-years	Incidence rate (1/100,000 person-years)	Model 1[a]	Model 2[b]	Model 3[c]
$PM_{2.5}$ exposure						
Low (≤65.02 μg/m^3)	2544	258,469	984.26	1.00	1.00	1.00
High (>65.02 μg/m^3)	2943	229,697	1281.25	1.50 (1.42–1.58)	2.18 (2.03–2.34)	1.98 (1.85–2.13)
$PM_{2.5}$ per 10 μg/m^3 increment				1.21 (1.19–1.24)	1.38 (1.35–1.42)	1.32 (1.29–1.36)
PA volume (MET-h/d)						
Q1 (≤16.0)	1742	138,023	1262.11	1.00	1.00	1.00
Q2 (>16.0–31.0)	1248	115,206	1083.28	0.83 (0.77–0.90)	0.82 (0.76–0.89)	0.90 (0.83–0.96)
Q3 (>31.0–52.0)	1235	122,452	1008.56	0.72 (0.67–0.78)	0.70 (0.65–0.76)	0.84 (0.78–0.91)
Q4 (>52.0)	1262	112,486	1121.92	0.76 (0.70–0.82)	0.73 (0.68–0.79)	0.90 (0.83–0.97)
P for trend				<0.001	<0.001	0.011
PA intensity (MET)						
Light (1.6–<3.0)	2324	197,642	1175.86	1.00	1.00	1.00
Moderate (3.0–<6.0)	1725	171,542	1005.58	0.75 (0.71–0.80)	0.76 (0.71–0.81)	0.81 (0.76–0.87)
Vigorous (≥6.0)	1266	109,407	1157.15	0.85 (0.79–0.91)	0.84 (0.78–0.91)	0.85 (0.79–0.92)
P for trend				<0.001	<0.001	0.091

Note: HR (95% CI) was calculated using Cox proportional hazards regression analysis stratified by cohort.

Abbreviations: MET, metabolic equivalent; PA, physical activity; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤ 2.5 μm; HR, hazard ratio; CI, confidence interval; Q, quartile; MET-h/d, MET-hours/day.

[a]Model 1 was adjusted for age and sex.

[b]Model 2 was further adjusted for urbanization, geographical region, education level, smoking status, alcohol drinking, and family history of type 2 diabetes.

[c]Model 3 was further adjusted for BMI, baseline blood glucose level, and $PM_{2.5}$ exposure (for the association with PA volume or average PA intensity) or PA volume (for the association with $PM_{2.5}$ exposure).

3.3 | Associations of PA with type 2 diabetes stratified by $PM_{2.5}$ exposure

Remarkably, substantial differences were observed in relationship between PA and type 2 diabetes across the low and high $PM_{2.5}$ exposure stratum (Figure 1). The higher PA volume was associated with a reduced risk of type 2 diabetes among participants exposed to low $PM_{2.5}$ exposure (Q2 vs. Q1 HR = 0.89, 95% CI: 0.80–0.99; Q3 vs. Q1 HR = 0.75, 95% CI: 0.67–0.85; Q4 vs. Q1 HR = 0.75, 95% CI: 0.66–0.85), whereas the higher PA volume was associated with an elevated risk of type 2 diabetes among participants exposed to high $PM_{2.5}$ exposure (Q2 vs. Q1 HR = 0.89, 95% CI: 0.80–0.99; Q3 vs. Q1 HR = 0.98, 95% CI: 0.88–1.09; Q4 vs. Q1 HR = 1.10, 95% CI: 0.99–1.22) (Supporting Information S1: Table 5). PA intensity exhibited a similar pattern when stratified by $PM_{2.5}$ exposure. In low $PM_{2.5}$ stratum, compared to light intensity of PA, we observed a 25% (HR = 0.75, 95% CI: 0.68–0.82) and 25% (HR = 0.75, 95% CI: 0.67–0.85) reduction in type 2 diabetes risk associated with moderate and vigorous intensity of PA, respectively, after full adjustment, while in high $PM_{2.5}$ stratum, fully adjusted HRs of moderate and vigorous intensity PA were 1.02 (95% CI: 0.92–1.12) and 1.13 (95% CI: 1.02–1.25), respectively (Supporting Information S1: Table 6). There was a significant interaction between $PM_{2.5}$ exposure and both PA volume and average PA intensity, with both $P_{interaction} < 0.001$ (Supporting Information S1: Tables 5 and 6).

3.4 | Combined effect of $PM_{2.5}$ exposure and PA on the risk of type 2 diabetes

Table 3 shows the combined impact of PA volume and intensity, along with $PM_{2.5}$ exposure, on the risk of type 2 diabetes. Participants exposed to high concentrations of $PM_{2.5}$ consistently showed a higher risk of type 2 diabetes compared to those exposed to low $PM_{2.5}$ stratification. A similar trend was observed for the relationship between PA intensity and type 2 diabetes at varying $PM_{2.5}$ exposure concentrations. Specifically, the combination of high $PM_{2.5}$ exposure and Q4 in PA volume (or vigorous intensity of PA) had the strongest association with type 2 diabetes risk, yielding a remarkable increase in risk of 79% (HR = 1.79, 95% CI: 1.59–2.01) and 82% (HR = 1.82, 95% CI: 1.64–2.02), respectively. When both $PM_{2.5}$ and PA volume (or average PA intensity) were treated as continuous variables, the bivariate response surface between $PM_{2.5}$ exposure and PA volume (or average PA intensity) was shown in Supporting Information S1: Figure 3.

3.5 | Sensitivity analysis

All sensitivity analyses regarding the influence of long-term $PM_{2.5}$ exposure to the association between PA volume (or average PA intensity) and incident type 2 diabetes was shown in Supporting Information S1: Tables 7–15. Sensitivity analyses did not reveal any significant changes, and we observed a robust and stable

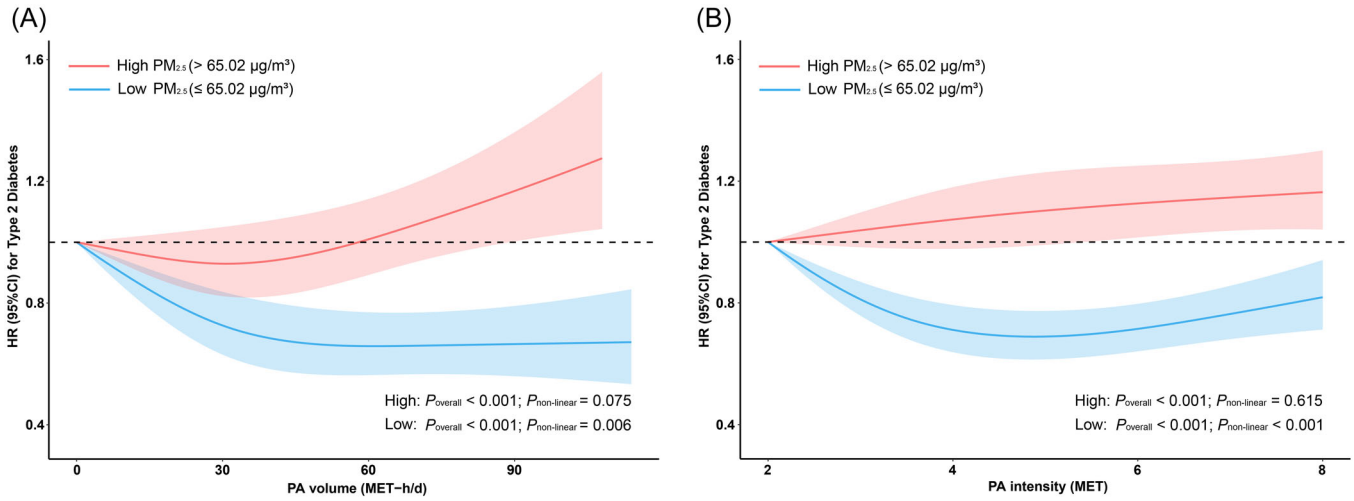

FIGURE 1 Exposure-response relations of PA with type 2 diabetes stratified by different levels of $PM_{2.5}$ exposure. The HRs for type 2 diabetes associated with PA volume (A) and PA intensity (B) were estimated by restricted cubic-spline regression under low and high levels of $PM_{2.5}$. Solid lines represent HRs, and the shaded areas represent 95% CIs. The models were adjusted for age, sex, urbanization, geographical region, education level, smoking status, alcohol drinking, family history of type 2 diabetes, BMI, and baseline blood glucose level. CI, confidence interval; HR, hazard ratio; MET, metabolic equivalent; MET-h/d, MET-hours/day; PA, physical activity; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm.

TABLE 3 The combined effects of $PM_{2.5}$ exposure and PA volume (or average PA intensity) on type 2 diabetes risk.

Subgroup	No. of cases	Person-years	Incidence/100,000 person-years	HR (95% CI)	*p* value
PA volume (MET-h/d)					
Low $PM_{2.5}$ exposure					
Q1 (≤16.0)	725	65,000	1115.39	Ref.	Ref.
Q2 (>16.0–31.0)	671	66,884	1003.23	0.89 (0.80–0.99)	0.033
Q3 (>31.0–52.0)	612	70,388	869.46	0.71 (0.63–0.80)	<0.001
Q4 (>52.0)	536	56,197	953.79	0.68 (0.60–0.77)	<0.001
High $PM_{2.5}$ exposure					
Q1 (≤16.0)	1017	73,023	1392.71	1.63 (1.46–1.83)	<0.001
Q2 (>16.0–31.0)	577	48,322	1194.08	1.40 (1.23–1.59)	<0.001
Q3 (>31.0–52.0)	623	52,064	1196.61	1.56 (1.38–1.77)	<0.001
Q4 (>52.0)	726	56,289	1289.78	1.79 (1.59–2.01)	<0.001
PA intensity (MET)					
Low $PM_{2.5}$ exposure					
Light (1.6–<3.0)	1157	109,367	1057.91	Ref.	Ref.
Moderate (3.0–<6.0)	862	97,908	880.42	0.71 (0.65–0.78)	<0.001
Vigorous (≥6.0)	463	47,877	967.05	0.69 (0.61–0.78)	<0.001
High $PM_{2.5}$ exposure					
Light (1.6–<3.0)	1167	88,275	1322.00	1.55 (1.41–1.72)	<0.001
Moderate (3.0–<6.0)	863	73,634	1172.01	1.57 (1.42–1.74)	<0.001
Vigorous (≥6.0)	803	61,530	1305.06	1.82 (1.64–2.02)	<0.001

Note: The Cox proportional hazard model was stratified by cohort and adjusted for age, sex, urbanization, geographical region, education level, smoking status, alcohol drinking, family history of type 2 diabetes, BMI, and baseline blood glucose level.

Abbreviations: CI, confidence interval; HR, hazard ratio; PA, physical activity; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; MET-h/d, MET-hours/day.

association between PA and type 2 diabetes risk across different stratifications of $PM_{2.5}$ exposure.

4 | DISCUSSION

This large-scale and population-based research conducted across China provided compelling evidence that long-term $PM_{2.5}$ exposure substantially reshaped the relationships of PA with the risk of type 2 diabetes. PA volume and intensity was inversely related to the risk of type 2 diabetes among individuals with lower concentrations of $PM_{2.5}$, whereas an elevated risk of type 2 diabetes was associated with greater levels of PA in those with higher $PM_{2.5}$ concentrations. Our research offers guidance to the Chinese population regarding reasonable exercise at higher levels of air pollution, filling an evidence gap in developing countries with serious air pollution.

Prior studies were primarily conducted in regions or countries with a lower concentration range of $PM_{2.5}$ and indicated that the benefits of PA outweighed the damage caused by increased inhalational dosage of $PM_{2.5}$ during PA. For instance, for the sake of solving this trade-off effects on diabetes, Kim et al. studied participants from the Korean National Health Insurance Service database (NHIS) and discovered that MVPA is associated with a decreased diabetes risk in groups exposed to both high and low/moderate levels of $PM_{2.5}$, with HRs of 0.95 (95% CI: 0.91–0.99) and 0.91 (95% CI: 0.89–0.94), respectively.[10] Similarly, a study from the UK Biobank demonstrated that the inverse association between PA and type 2 diabetes remained relatively stable across varying concentrations of $PM_{2.5}$. Specifically, there was a reduction in the risk of type 2 diabetes by 0.28%, 0.27%, and 25% in high PA under low, moderate, and high concentrations of $PM_{2.5}$, respectively.[11] Habitual PA could mitigate the risk of diabetes irrespective of $PM_{2.5}$ concentrations, which was observed in a longitudinal cohort study from Taiwan, China.[26] The studies mentioned above were conducted in relatively favorable air quality, with average $PM_{2.5}$ concentrations mostly below 30 $\mu g/m^3$. Even the highest $PM_{2.5}$ levels observed in some studies did not reach the lowest concentrations in

our study, potentially limiting their applicability to high-concentration areas. Besides, despite a study from southwestern China covering a wider spectrum of $PM_{2.5}$ concentrations, it only investigated the correlation between PA and type 2 diabetes under different levels of $PM_{2.5}$ in a cross-sectional perspective, thereby failing to establish a causal relationship.[9] However, our study not only featured a wide range of $PM_{2.5}$ exposure (ranging from 31.17 to 88.84 μg/m^3) across diverse regions in China but also adopted a cohort study design. In our observation, the beneficial effect of PA on type 2 diabetes has shifted to a detrimental one under severe air pollution conditions.

Former studies failed to cover wider ranges of $PM_{2.5}$ levels or offer a comprehensive evaluation of PA. Although previous research explored the relationship between PA and health in various levels of air pollution, they mainly assessed PA in terms of frequency, type, and volume, with less attention on intensity. Notably, recent guidelines of PA emphasized the imperative for research in this area.[13,27] Previous studies have shown that MVPA mostly reduces the risk of type 2 diabetes.[28,29] An up-to-date UK biobank study suggested that compared with low-intensity physical activity (LPA), MVPA has the stronger correlation with the risk of developing type 2 diabetes.[29] Further analysis stratified by the median $PM_{2.5}$ concentration in our study revealed that heightened PA intensity provided stronger protection against type 2 diabetes in areas with lower $PM_{2.5}$ levels; while with increasing $PM_{2.5}$ concentrations, the association between PA and type 2 diabetes transitioned from being beneficial to detrimental. In addition, we were the first to identify a significant interaction between PA intensity and $PM_{2.5}$ exposure on type 2 diabetes incidence rates.

The protective effects of PA on diabetes occur via a variety of mechanisms, including increased cardiorespiratory endurance, higher lipid levels, improved endothelial function,[7] stimulation of anti-inflammatory signaling pathways,[30] and enhanced insulin sensitivity.[31] In addition, we observed that when $PM_{2.5}$ concentration exceeded the median (65.02 μg/m^3), both the volume and intensity of PA failed to confer protection against type 2 diabetes, showing an adverse effect instead. The plausible explanations for this were that PA may increase the absorption of airborne pollutants owing to heightened ventilation rate, escalated deposition fraction within the respiratory tract, and transitioning from nasal to oral respiration.[32] Besides, the amount of air contaminants inhaled may increase with higher PA intensity. Saber et al. explained this phenomenon by demonstrating a direct relationship between heightened respiratory exertion and an amplified deposition ratio of particles within all respiratory regions, irrespective of particle size.[33] Similarly, a study further evaluated the amount of particulate matter (PM) deposited in the airways, indicating particle deposition in the airway enhanced 3.0- to 4.5-fold after light exercise and 6- to 10-fold after intense exercise.[34]

How to balance the trade-off effects of air pollution exposure and PA is still a strongly discussed scientific topic. This study found that elevated concentrations of $PM_{2.5}$ exposure may attenuate the beneficial effects of PA on type 2 diabetes and could potentially exacerbate its onset. Consequently, advocating for reduced outdoor activities to mitigate health risks in highly polluted regions emerges as a pragmatic interim measure. However, this approach is inherently transient and necessitates collaborative efforts from policymakers, environmental experts, and the public to implement air quality management strategies for sustainable improvements. Currently, China has achieved periodical progress in the regulation of air pollution. The annual average $PM_{2.5}$ concentration in China has decreased from 72 μg/m^3 in 2013[35] to 29 μg/m^3 in 2022.[36] However, there is still a long way to reach the more stringent Air Quality Guidelines (AQG) standard for $PM_{2.5}$ concentrations set by the World Health Organization (WHO) in 2021, which has been reduced from the annual average of 10 μg/m^3 in 2005 to 5 μg/m^3 in 2021.[37] Our study not only provided scientifically sound recommendations on PA under different levels of $PM_{2.5}$ exposure but also highlighted the urgency of stronger regulations and strategies for future air pollution reduction.

Our study has several merits. To our knowledge, this is the first study to examine the association between PA and type 2 diabetes in a large prospective Chinese cohort across various levels of $PM_{2.5}$ exposure. Second, a high-precision satellite-based spatiotemporal model was used to evaluate $PM_{2.5}$ concentrations in China, and the $PM_{2.5}$ exposure encompassed a broader range of concentrations, potentially providing supplementary evidence for high exposures in the dose–response relationship. Another merit was that our study benefitted from an extended follow-up period, detailed baseline and follow-up information, and rigorous standardized protocols. However, this study has a few limitations. First, the residences of individuals might not match with their primary activity locations, potentially leading to some misclassification in assessing $PM_{2.5}$ exposure. Second, the absence of specific inquiries about indoor and outdoor activities in the questionnaire hindered us from thoroughly investigating the indoor PA. Third, air contaminants, other climatic conditions, and ambient noise were not accounted for in our statistical modeling due to the unavailability of high-quality and high-resolution exposure data.

In conclusion, our prospective cohort study revealed that high $PM_{2.5}$ exposure might diminish the protective benefits of regular PA against the development of type 2 diabetes. Consequently, safety and health benefits of PA should be comprehensively evaluated for people living in heavily polluted areas to prevent type 2 diabetes.

AUTHOR CONTRIBUTION

Qian Li, Formal analysis, visualization, writing—original draft and review and editing. **Fangchao Liu**, Methodology, data curation, writing—review and editing. **Keyong Huang**, Methodology, data curation, writing—review and editing. **Fengchao Liang**, Methodology. **Chong Shen**, Investigation, writing—review and editing, funding acquisition. **Jian Liao**, Writing—review and editing. **Jianxin Li**, Data curation, investigation. **Chenxi Yuan**, Writing—review and editing. **Xueli Yang**, Investigation. **Jie Cao**, Investigation. **Shufeng Chen**, Investigation. **Dongsheng Hu**, Investigation. **Jianfeng Huang**, Investigation, funding acquisition. **Yang Liu**, Methodology. **Xiangfeng Lu**, Investigation, supervision, funding acquisition. **Dongfeng Gu**, Conceptualization, methodology, supervision, funding acquisition. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. Professor Xiangfeng Lu and Dongfeng Gu are members of Chronic Diseases and Translational Medicine editorial board and are not involved in the peer review and decision process of this article.

DATA AVAILABILITY STATEMENT

Data will be made available on request.

ETHICS STATEMENT

The China-PAR project received approval from the Ethics Committee of Fuwai Hospital in Beijing, China and the ethical approval number was 2012-399.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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