

## Research Paper

## Ambient fine particulate matter constituents and semen quality among adult men in China

Yangchang Zhang<sup>a,1</sup>, Jing Wei<sup>b,1</sup>, Shi Zhao<sup>c</sup>, Qiang Zeng<sup>d,e,\*</sup>, Shengzhi Sun<sup>a,f,g,h,\*\*</sup>, Wangnan Cao<sup>i,\*\*\*</sup>

<sup>a</sup> School of Public Health, Capital Medical University, Beijing 100069, China

<sup>b</sup> Department of Atmospheric and Oceanic Science, Earth System Science Interdisciplinary Center, University of Maryland, College Park, MD 20740, USA

<sup>c</sup> Centre for Health Systems and Policy Research, Chinese University of Hong Kong, 999077, the Hong Kong Special Administrative Region of China

<sup>d</sup> Department of Occupational and Environmental Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

<sup>e</sup> Key Laboratory of Environment and Health, Ministry of Education & Ministry of Environmental Protection, State Key Laboratory of Environmental Health (incubating), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

<sup>f</sup> Beijing Municipal Key Laboratory of Clinical Epidemiology, Capital Medical University, Beijing 100069, China

<sup>g</sup> Beijing Laboratory of Allergic Diseases and Beijing Key Laboratory of Nasal Diseases, Beijing Institute of Otolaryngology, Beijing 100005, China

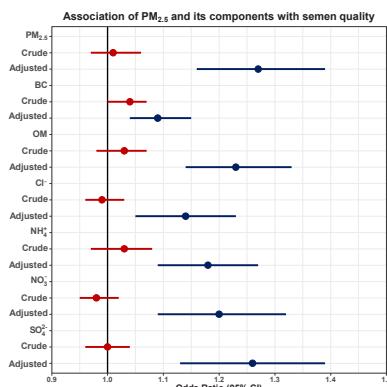
<sup>h</sup> School of Public Health, The Key Laboratory of Environmental Pollution Monitoring and Disease Control, Ministry of Education, Guizhou Medical University, Guiyang, 550025, China

<sup>i</sup> Department of Social Medicine and Health Education, School of Public Health, Peking University, Beijing 100191, China

## HIGHLIGHTS

- Evidence on the association between PM<sub>2.5</sub> constituents and semen quality is limited.
- Exposure to OM, BC, Cl<sup>-</sup>, or NO<sub>3</sub><sup>-</sup> was associated with a decline in semen quality.
- The association was more pronounced among older men and individuals with lower levels of education.

## GRAPHICAL ABSTRACT



\* Corresponding author at: Department of Occupational and Environmental Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China.

\*\* Corresponding author at: School of Public Health, Capital Medical University, Beijing 100069, China

\*\*\* Corresponding author.

E-mail addresses: [zengqiang506@hust.edu.cn](mailto:zengqiang506@hust.edu.cn) (Q. Zeng), [shengzhisun@ccmu.edu.cn](mailto:shengzhisun@ccmu.edu.cn) (S. Sun), [wangnancao@bjmu.edu.cn](mailto:wangnancao@bjmu.edu.cn) (W. Cao).

<sup>1</sup> These authors contributed equally to this work.

## ARTICLE INFO

Editor: Yuming Guo

**Keywords:**  
Semen quality  
Chinese men  
PM constituents

## ABSTRACT

Exposure to ambient fine particulate matter ( $PM_{2.5}$ ) was associated with decreased semen quality, but the relationship between  $PM_{2.5}$  constituents and semen quality was unclear. We recruited 27,824 adult men attending an infertility clinic in Wuhan, China, between 2014 and 2020. We used a four-dimensional spatio-temporal deep forest model to estimate concentrations of  $PM_{2.5}$  mass and its chemical constituents, including organic matter (OM), black carbon (BC), sulfate ( $SO_4^{2-}$ ), nitrate ( $NO_3^-$ ), ammonium ( $NH_4^+$ ), and chloride ( $Cl^-$ ). We employed linear regression models to estimate the association between  $PM_{2.5}$  mass and its constituents with various sperm parameters. Exposure to  $PM_{2.5}$  was associated with a reduction in sperm quality, with a percent change of  $-5.69\%$  (95% confidence interval [CI]:  $-8.53\%, -2.85\%$ ) for sperm density,  $-15.09\%$  (95% CI:  $-22.24\%, -7.94\%$ ) for sperm total count,  $-1.63\%$  (95% CI:  $-2.36\%, -0.91\%$ ) for sperm progressive motility, and  $-2.30\%$  (95% CI:  $-3.04\%, -1.55\%$ ) for sperm total motility. Among specific constituents, exposure to OM, BC,  $Cl^-$ , or  $NO_3^-$  was associated with a reduction in these four semen quality parameters. The association was more pronounced among older men or individuals with lower levels of education. Our findings suggest that  $PM_{2.5}$  mass and each constituent were associated with decreased semen quality in adult men.

## 1. Introduction

Over the past decades, there has been a concerning decline in semen quality [16]. A recent meta-analysis of 44 epidemiological studies has revealed a substantial global reduction in sperm density and sperm count, with an annual decline of 0.87 million/mL and 62.3% between 1973 and 2018 [16]. This decline is alarming, considering that approximately half of infertility cases could be attributed to suboptimal sperm quality, affecting around 10% of couples worldwide [9].

Emerging studies have suggested that exposure to ambient fine particulate matter ( $PM_{2.5}$ ) was linked with semen quality decline, but results have been mixed [41,42,6,7]. For example, a recent meta-analysis detected a relatively high heterogeneity in the associations between exposure to  $PM_{2.5}$  and semen quality across 22 epidemiological studies [39]. The differences in these associations could be largely attributed to differences in study populations, methodologies for exposure assessment, the statistical analysis approaches employed, and particulate matter (PM) constituents [19]. The toxicity of  $PM_{2.5}$  is primarily driven by its chemical constituents, which vary widely across regions, seasons, and pollution sources [26]. However, there is limited evidence examining the association between PM chemical constituents and semen quality.

Accordingly, we sought to estimate the association between exposure

to  $PM_{2.5}$  mass and its constituents and various semen quality parameters (i.e., sperm density, sperm count, sperm progressive motility, and sperm total motility) among 27,824 participants attending an infertility clinic in Hubei province, China.

## 2. Materials and methods

## 2.1. Study setting and population

We conducted a cross-sectional study and recruited adult men who attended the Reproductive Medical Center, Tongji Hospital in Wuhan, China, between January 2014 and December 2020. We included participants with detailed residential locations and air pollution data ( $n = 32,381$ ). We excluded 4557 participants with known diseases or conditions associated with male reproductive dysfunction. Examples of such conditions include self-reported azoospermia, vasectomy, epididymitis, vesiculitis, varicocele, injury of the testis, and endocrine disease. After this exclusion, we included 27,824 participants in the final analytical framework. The spatial distribution of the included participants was shown in Fig. 1.

We used a standard structured questionnaire to collect individual's baseline characteristics. Clinical examinations were conducted by specialized nurses. We calculated the body mass index (BMI) using the

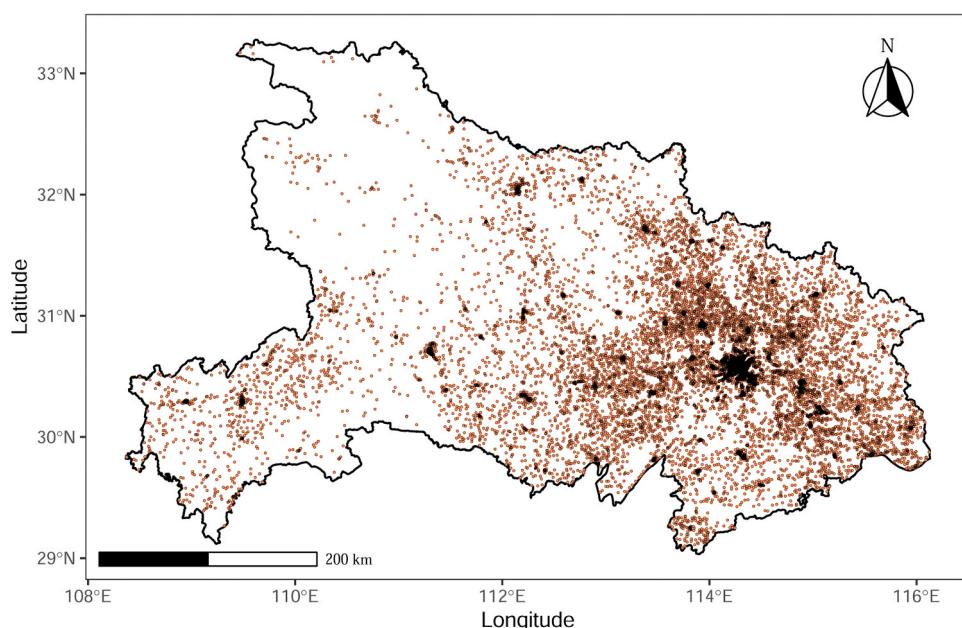


Fig. 1. Spatial distribution of the included study participants ( $n = 27,824$ ).

participant's weight in kilograms divided by the square of their height in meters. The data collection has been detailed elsewhere [30,40]. This study was approved by the Ethics Committee of Tongji Medical College (approval ID: 2019(s004)).

## 2.2. Semen sample collection

The methodology for semen collection was described elsewhere [30]. Participants were instructed to abstain from sexual activity for a designated period and then masturbate into a sterile plastic specimen container in a designated room. Following collection, the semen was liquefied in a heating chamber for a maximum duration of 60 min, after which it was tested for semen quality. The definition of semen quality was based on key parameters, including sperm density, sperm total count, sperm progressive motility, and sperm total motility. Semen volume (measured in mL) was estimated using a serologic pipette. Sperm density ( $10^6/\text{mL}$ ) and sperm motility (i.e., progressive and total motility [%]) were quantified through a computer-aided semen analysis system. The total sperm count ( $10^6$ ) was calculated by multiplying semen volume by sperm density. Additionally, total motility was calculated by summing progressive and non-progressive motility. For standardization and consistency, all procedures followed the guidelines outlined in the World Health Organization (WHO) laboratory manual for the examination and processing of human semen (5th edition) [35].

## 2.3. Exposure assessment

We geocoded residential addresses of each participant into latitude and longitude coordinates, which were used to match the estimates from the  $1 \times 1 \text{ km}$  grid cells from the ChinaHighAirPollutants (CHAP) dataset (<https://weijing-rs.github.io/product.html>). CHAP dataset is derived from multidimensional data using a machine learning approach, including ground-based measurements, satellite remote sensing products, atmospheric reanalysis, and model simulations [33,31,32]. This dataset offers long-term, full-coverage, high-resolution data, and has been widely used to assess the adverse effects of air pollution [33,36]. Within the CHAP dataset, PM<sub>2.5</sub> constituents were estimated using a sophisticated four-dimensional spatiotemporal deep forest model at a spatial resolution of 1 km. The estimates include back carbon (BC), sulfate ( $\text{SO}_4^{2-}$ ), nitrate ( $\text{NO}_3^-$ ), ammonium ( $\text{NH}_4^+$ ), and chloride ( $\text{Cl}^-$ ). High predictive accuracy was verified via cross-validation for BC,  $\text{SO}_4^{2-}$ ,  $\text{NO}_3^-$ ,  $\text{NH}_4^+$ , and  $\text{Cl}^-$  concentrations when compared to ground-based observations, with coefficients of determination of 0.82, 0.73, 0.75, 0.71 and 0.66, and average root-mean-square errors (RMSE) of 1.64, 6.0, 6.6, 4.3, and  $2.3 \mu\text{g}/\text{m}^3$ , respectively [33,34]. As the concentrations of organic matter (OM) cannot be directly measured, we calculated them approximately by subtracting the sum of BC,  $\text{SO}_4^{2-}$ ,  $\text{NO}_3^-$ ,  $\text{NH}_4^+$ , and  $\text{Cl}^-$  concentrations from the total PM<sub>2.5</sub> mass concentrations.

In addition, we obtained daily data on ambient temperature and relative humidity from the meteorological bureau of China. To estimate the meteorological conditions at each individual's location, we applied the inverse distance weighting method, utilizing data from the three nearest monitoring stations [8].

For each participant, we calculated the average concentration of PM<sub>2.5</sub> constituents and meteorological variable during the entire sperm development period (0–90 days before semen collection) or during each specific essential period of sperm development, including epididymal storage (0–9 days before semen collection), sperm motility development (10–14 days before semen collection), and spermatogenesis (70–90 days before semen collection) [5].

## 2.4. Statistical analysis

We initially examined the correlation between PM<sub>2.5</sub> mass and its individual constituent using Pearson correlation coefficients. Correlation coefficients exceeding 0.8 were considered as indicative of a strong

correlation.

We used multivariate linear regression models to examine the association of semen quality parameters with PM<sub>2.5</sub> mass and its five chemical constituents during the entire sperm development (0–90 days). For the crude model, we adjusted for calendar year of sperm collection. For the fully adjusted model, we additionally adjusted for age ( $\leq 30$ , 31–39,  $\geq 40$  years, unknown), BMI ( $< 18.5$ , 18.5–23.9,  $\geq 28.0 \text{ kg}/\text{m}^2$ , unknown), education (college and higher, high school, middle school and lower, unknown), ever having fathered a child (yes, no, unknown), and season of sperm collection (spring [March to May], summer [June to August], autumn [September to November], and winter [December to February]), daily mean ambient temperature, and relative humidity based on previous studies [27,41,42]. We expressed results as beta coefficients and 95% confidence intervals (CIs) for each sperm quality parameter associated with an interquartile range (IQR) increase in PM<sub>2.5</sub> constituents. To address right-skewed data, such as sperm density and sperm total count, we applied logarithmic transformations to approximate a Gaussian distribution before model fitting.

To examine the relationship between PM<sub>2.5</sub> constituents and semen quality parameters, we used restricted cubic spline functions for PM<sub>2.5</sub> constituents, and adjusted for the same covariates as in the fully adjusted models [29,41]. We evaluated the potential nonlinearity through visual inspection and likelihood ratio tests comparing models incorporating restricted cubic spline term and linear term for exposures [3].

To explore the susceptible exposure windows, we conducted additional analysis to examine whether the association was varied by three key periods of sperm development, including epididymal storage, sperm motility development, and spermatogenesis.

To identify susceptible subpopulations, we conducted stratified analyses by age ( $\leq 33$  versus  $> 33$  years [median]), education (high school and lower versus college and higher), and BMI ( $< 24$  versus  $\geq 24 \text{ kg}/\text{m}^2$ ). We used two-sample Student's *t* test to assess the differences between coefficients in these subgroups [12].

We performed four main sensitivity analyses to confirm the robustness of our findings. First, to assess the detrimental effects of PM<sub>2.5</sub> exposure in comparison with unequal semen quality degrees, we categorized participants into normal and abnormal groups based on WHO guideline. The reference values for the normal group were sperm density greater than  $15 \times 10^6/\text{mL}$ , sperm count greater than  $39 \times 10^6$ , and total and progressive motility above 40% and 32% motile sperms, respectively. Conversely, the abnormal group consisted of participants who fell below any of the aforementioned reference values. Then, we fitted logistic regression with the same covariates mentioned above to explore whether exposure to PM<sub>2.5</sub> mass and its constituents was associated with declined in semen quality between normal and abnormal semen group. Second, to assess whether the effects of PM<sub>2.5</sub> constituents were also observed in men with normal semen quality, we conducted stratified analysis and repeated the main analyses in normal semen group. Third, to assess the independent effects of each PM<sub>2.5</sub> constituent, we conducted the two-constituent model included 1 PM<sub>2.5</sub> constituent at a time into the model when the Pearson correlation between the constituent of interest and the co-constituent was below 0.80 to avoid collinearity. Fourth, to consider the nonlinear effects of ambient temperature and relative humidity, we adjusted for ambient temperature and relative humidity using a natural cubic spline. The degree of freedom for the natural cubic spline in relation to ambient temperature and relative humidity was guided by selecting the minimum Akaike information criterion of model fitting.

All statistical analyses were conducted in R software (version 4.2.1). We corrected for multiple testing in the models by applying Benjamini-Hochberg false discovery rate (FDR) and set the false positive threshold as 5% [21,4].

### 3. Result

#### 3.1. Descriptive results

During the study period, a total of 27,824 adult men were enrolled in the study. Most participants fell within the age range of 31 to 39 years (53.3%) (Table 1). The median values for sperm density, sperm total count, progressive motility, and total motility were  $52.0 \times 10^6/\text{mL}$ ,  $130.0 \times 10^6$ , 42.1%, and 47.0%, respectively (Table 1). The mean concentrations of PM<sub>2.5</sub> mass, OM, BC, Cl<sup>-</sup>, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>, and NO<sub>3</sub><sup>-</sup> were 47.7, 16.7, 3.8, 1.2, 10.8, 6.1, and 9.0  $\mu\text{g}/\text{m}^3$ , respectively (Table 2). The average relative humidity and ambient temperature was 77.2% and 20 °C, respectively (Table 2). We found that PM<sub>2.5</sub> and its constituents are highly correlated (Pearson correlation > 0.8) (Fig. S1).

#### 3.2. Regression Results

We found that exposure to PM<sub>2.5</sub> mass and specific constituents during the entire sperm development was associated with a decline in sperm quality. For example, each IQR ( $28.3 \mu\text{g}/\text{m}^3$ ) increase in PM<sub>2.5</sub> mass concentration was associated with a reduction of -5.69% (95% CI: -8.53%, -2.85%) in sperm density, -15.09% (95% CI: -22.24%, -7.94%) in sperm total count, -1.63% (95% CI: -2.36%, -0.91%) in

**Table 1**

The demographic characteristics and sperm quality parameters of the included participants ( $n = 27,824$ ).

Variables	N (%)
	Median (IQR)
<b>Age (year)</b>	
≤ 30	8698 (31.3%)
31-39	14823 (53.3%)
≥ 40	4302 (15.5%)
Unknown	1 (0.0%)
<b>BMI (<math>\text{kg}/\text{m}^2</math>)</b>	
< 18.5	1101 (4.0%)
18.5-23.9	12813 (46.1%)
24.0-27.9	10404 (37.4%)
≥ 28.0	3225 (11.6%)
Unknown	281 (1.0%)
<b>Educational levels</b>	
College and higher	12386 (44.5%)
High school	3347 (12.0%)
Middle school and lower	12070 (43.4%)
Unknown	21 (0.1%)
<b>Ever having fathered a child</b>	
No	13435 (48.3%)
Yes	3974 (14.3%)
Unknown	10415 (37.4%)
<b>Sperm quality parameters</b>	
Sperm density ( $10^6/\text{mL}$ )	52.0 (38.0)
Sperm count ( $10^6$ )	130.0 (148.6)
Progressive motility (%)	42.1 (24.0)
Total motility (%)	47.0 (25.0)
<b>Season<sup>a</sup></b>	
Spring	6402 (23.0%)
Summer	9079 (32.6%)
Autumn	7297 (26.2%)
Winter	5046 (18.1%)
<b>Year<sup>b</sup></b>	
2014	3431 (12.3%)
2015	3701 (13.3%)
2016	4232 (15.2%)
2017	4518 (16.2%)
2018	4499 (16.2%)
2019	4779 (17.2%)
2020	2664 (9.6%)

Note. Abbreviation: BMI, Body mass index; IQR, Interquartile range.

<sup>a</sup> Season of semen collection was defined as Spring (March to May), Summer (June to August), Autumn (September to November), and Winter (December to February).

<sup>b</sup> Year of semen collection.

**Table 2**

Summary statistics of daily average ambient PM<sub>2.5</sub> and its constituents among 27,824 participants in Hubei, China.

Air pollutant ( $\mu\text{g}/\text{m}^3$ )	Mean	SD	Median	Min	P <sub>25</sub>	P <sub>75</sub>	Max
PM <sub>2.5</sub>	47.7	18.9	44.5	11.8	32.1	60.4	153.7
OM	16.7	8.8	15.1	0.0	9.6	22.6	75.1
BC	3.8	1.2	3.6	0.9	2.9	4.6	9.6
Cl <sup>-</sup>	1.2	0.6	1.1	0.3	0.7	1.6	6.4
SO <sub>4</sub> <sup>2-</sup>	10.8	2.5	10.4	4.1	8.9	12.6	25.9
NH <sub>4</sub> <sup>+</sup>	6.1	2.0	5.9	1.8	4.5	7.4	16.3
NO <sub>3</sub> <sup>-</sup>	9.0	4.8	7.9	2.0	5.0	12.2	27.9
Relative humidity (%)	77.1	4.1	77.2	56.7	74.6	79.9	91.1
Ambient temperature (°C)	18.9	6.8	20	2.5	13.3	25.1	29.4

Abbreviations: PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter  $\leq 2.5 \mu\text{m}$ ; OM, organic matter; BC, black carbon; SO<sub>4</sub><sup>2-</sup>, sulfate; NO<sub>3</sub><sup>-</sup>, nitrate; NH<sub>4</sub><sup>+</sup>, ammonium; Cl<sup>-</sup>, chloride.

progressive motility, and -2.30% (95% CI: -3.04%, -1.55%) in total motility (Fig. 2).

For PM<sub>2.5</sub> constituents, we found that exposure to BC, OM, Cl<sup>-</sup>, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>, and NO<sub>3</sub><sup>-</sup> were all significantly associated with decreased sperm density (Fig. 2). For example, each IQR increase in BC, OM, Cl<sup>-</sup>, NH<sub>4</sub><sup>+</sup>, NO<sub>3</sub><sup>-</sup>, and SO<sub>4</sub><sup>2-</sup> was associated with a reductions of -1.89% (95% CI: -3.50%, -0.28%), -4.48% (95% CI: -6.91%, -2.05%), -3.32% (95% CI: -5.97%, -0.68%), -5.48% (95% CI: -8.51%, -2.45%), -4.31% (95% CI: -7.56%, -1.05%) and -5.94% (95% CI: -8.32%, -3.55%) in sperm density, respectively.

To explore susceptible exposure windows, we estimated the association separately for each essential period of sperm development (Table 3). We found that the association was generally more pronounced during spermatogenesis (70–90 days before semen collection). For example, the sperm total count dropped by -8.74% (95% CI: -13.74%, -3.75%) associated with an IQR increase in SO<sub>4</sub><sup>2-</sup> during the lag period of 70–90 days, compared to -0.35% (95% CI: -3.36%, 2.66%) during the lag period of 10–14 days, and -3.41% (95% CI: -6.83%, 0.02%) during the lag period of 0–9 days before semen collection.

#### 3.3. Exposure-response relationship

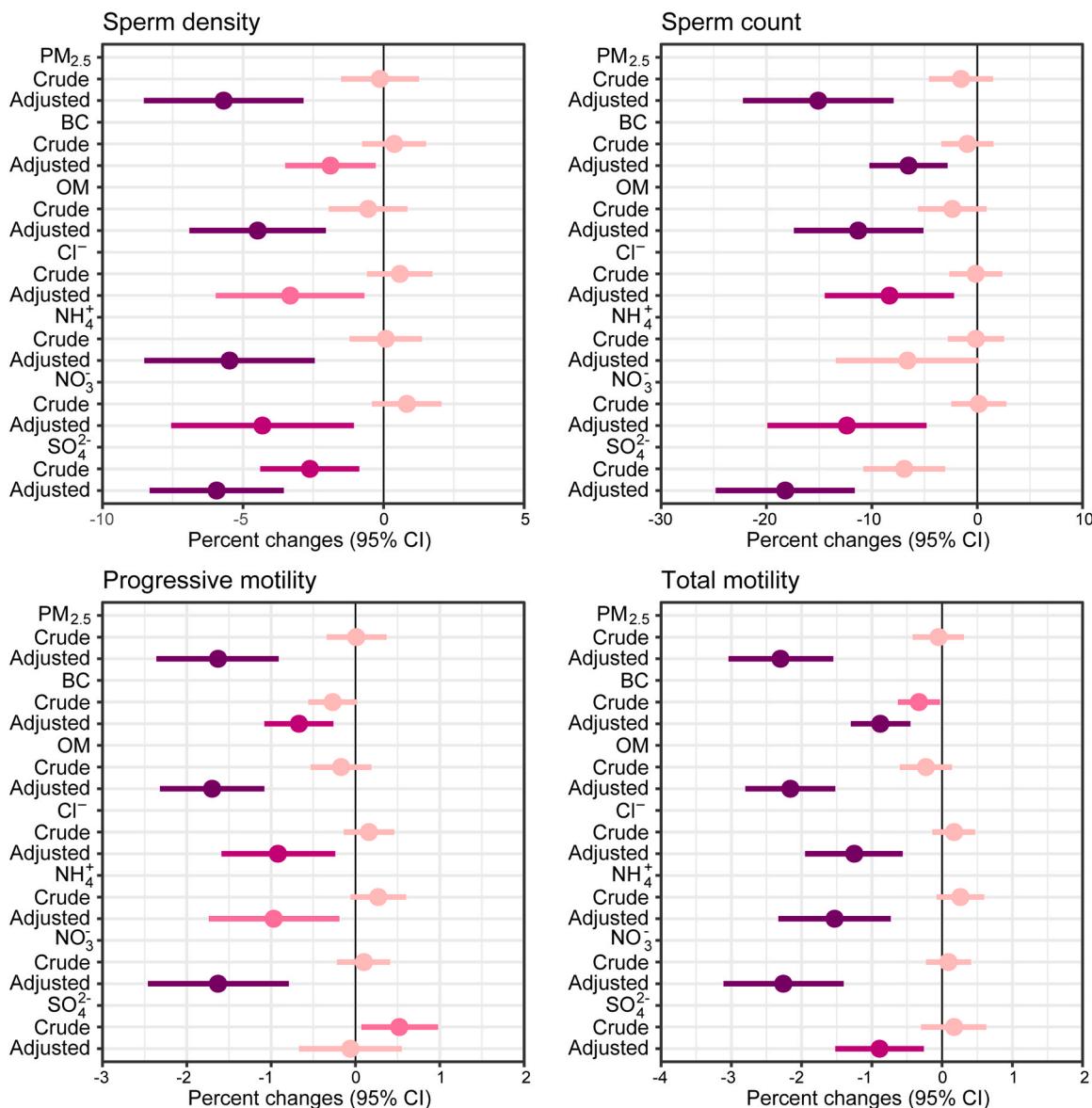
To examine the exposure-response relationship between PM<sub>2.5</sub> mass and its constituents and semen quality, we used a restricted cubic spline function for PM<sub>2.5</sub> mass and each constituent, and adjusted for the same covariates as in the fully adjusted models. We found an approximate linear relationship between PM<sub>2.5</sub> or BC and four semen quality parameters. However, when considering other constituents like OM, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>, Cl<sup>-</sup>, and NO<sub>3</sub><sup>-</sup>, we identified nonlinear associations with specific semen parameters (Fig. 4).

#### 3.4. Subgroup analyses

To examine vulnerable subpopulations, we conducted subgroup analyses by age, education, and BMI. We found that the association was more pronounced among men aged above 33 years or those with a high school education or lower. Specifically, for sperm total count, we found a reduction of -15.51% (95% CI: -24.31%, -6.71%) among men aged above 33 years compared to -13.60% (95% CI: -22.73%, -4.47%) among men aged younger than 33 years, associated with an IQR increase in Cl<sup>-</sup> (Fig. 3, Table S1, and Table S2).

#### 3.5. Sensitivity analysis

We investigated the effects estimation of PM<sub>2.5</sub> and its constituents in comparison with normal and abnormal semen quality group. We found that exposure to PM<sub>2.5</sub> and its constituents during the entire period of



**Fig. 2.** Percent change of sperm quality associated with an interquartile range increase in daily concentration of PM<sub>2.5</sub> constituents during the entire sperm development. Note: Crude: Crude model only included survey calendar year in the models; Adjusted: Fully adjusted models additionally adjusted for age, body mass index, educational levels, ever having fathered a child, daily mean ambient temperature, relative humidity, year and season of semen collection. Abbreviations: PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter  $\leq 2.5 \mu\text{m}$ ; BC, black carbon; OM, organic matters; SO<sub>4</sub><sup>2-</sup>, sulfate; NO<sub>3</sub>, nitrate; NH<sub>4</sub><sup>+</sup>, ammonium; Cl<sup>-</sup>, chloride.

sperm development was associated with increased odds of abnormal semen quality condition (Table S3). To assess the independent effects of each chemical constituents, we constructed two-constituent models, and we found that the magnitude of the estimates were not materially different from those in the single constituent models (Table S4). Our findings remained consistent among men with normal semen quality (Table S5) or after adjusting for ambient temperature and relative humidity using a natural cubic spline (Table S6).

#### 4. Discussion

In this cross-sectional study of 27,824 adult men from Hubei, China, we found that each PM<sub>2.5</sub> constituents, including BC, OM, Cl<sup>-</sup>, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>, and NO<sub>3</sub>, was associated with a reduction in semen quality. We found that the association was more pronounced among men aged 33 years or older or those with a high school education or lower.

Leveraging high-resolution PM<sub>2.5</sub> constituents gridded data, we

found that exposure to PM<sub>2.5</sub> mass was inversely associated with sperm density, sperm total count, sperm progressive motility, and sperm total motility, which were consistent with previous studies [38,42,7]. For example, Zhao et al. conducted a population-based retrospective study involving 33,876 men in China, reporting that an interquartile range increase in PM<sub>2.5</sub> exposures were associated with a decrease of  $-3.60\%$  (95% CI:  $-3.93\%$ ,  $-3.26\%$ ) in sperm total motility and  $-1.87\%$  (95% CI:  $-2.37\%$ ,  $-1.36\%$ ) in sperm progressive motility [42].

PM<sub>2.5</sub> is a complex mixture comprising various chemical constituents, including carbonaceous fractions, transition metals, and ions, each potentially contributing adverse effects on semen quality [14]. Therefore, it is crucial to examine the individual effects of these specific constituents.

Our findings indicated that exposure to BC and OM were associated with declines in all four sperm quality parameters, including sperm density, sperm total count, sperm progressive motility, and sperm total motility. To our best knowledge, no prior study has examined this

**Table 3**

Effect estimates of semen quality parameters associated with an interquartile range increase in PM<sub>2.5</sub> mass and its constituents during specific time windows of sperm development.

Exposure time window, lag days <sup>b</sup>	Effect estimate (95% CI) <sup>a</sup>			
	Sperm density (10 <sup>6</sup> /mL)	Sperm count (10 <sup>6</sup> )	Progressive motility (%)	Total motility (%)
PM <sub>2.5</sub> , µg/m <sup>3</sup>				
0-9	0.59 (-1.03, 2.22)	0.41 (-3.70, 4.52) -0.21	-0.63 (-1.04, -0.21)	-0.82 (-1.25, -0.39)
10-14	-0.47 (-1.83, 0.89)	1.23 (-2.10, 4.57) 0.19	-0.15 (-0.50, 0.19)	-0.18 (-0.54, 0.18)
70-90	-0.91 (-3.11, 1.29)	-6.94 (-13.05, -0.83)	-0.55 (-1.11, 0.02)	-0.79 (-1.37, -0.21)
BC, µg/m <sup>3</sup>				
0-9	0.59 (-0.66, 1.84)	-0.18 (-3.01, 2.66) -0.29	-0.61 (-0.93, -0.29)	-0.76 (-1.09, -0.43)
10-14	0.24 (-0.87, 1.35)	0.38 (-2.10, 2.87) 0.04	-0.25 (-0.53, 0.04)	-0.31 (-0.60, -0.01)
70-90	-0.03 (-1.42, 1.36)	-3.34 (-6.67, 0.00) 0.00	-0.35 (-0.71, 0.00)	-0.39 (-0.76, -0.03)
OM, µg/m <sup>3</sup>				
0-9	0.74 (-0.73, 2.21)	0.51 (-3.20, 4.23) -0.31	-0.69 (-1.06, -0.31)	-0.84 (-1.23, -0.45)
10-14	-0.61 (-1.88, 0.65)	0.49 (-2.59, 3.56) 0.10	-0.22 (-0.55, 0.10)	-0.25 (-0.58, 0.09)
70-90	-0.82 (-2.77, 1.13)	-3.59 (-8.96, 1.79) -0.28	-0.78 (-1.28, -0.28)	-0.95 (-1.47, -0.44)
Cl <sup>-</sup> , µg/m <sup>3</sup>				
0-9	0.07 (-1.98, 2.12)	-2.05 (-7.19, 3.08) 0.09	-0.44 (-0.96, -0.31)	-0.59 (-1.13, -0.04)
10-14	-0.09 (-1.82, 1.65)	1.62 (-2.81, 6.05) 0.43	-0.02 (-0.46, 0.43)	-0.03 (-0.49, 0.42)
70-90	-0.20 (-2.20, 1.80)	-3.88 (-9.45, 1.70) 0.44	-0.07 (-0.59, 0.44)	-0.20 (-0.72, 0.33)
SO <sub>4</sub> <sup>2-</sup> , µg/m <sup>3</sup>				
0-9	-0.49 (-1.64, 0.66)	-3.41 (-6.83, 0.02) 0.30	0.01 (-0.29, 0.30)	-0.15 (-0.46, 0.15)
10-14	-0.37 (-1.42, 0.69)	-0.35 (-3.36, 2.66) 0.59	0.32 (0.05, 0.59)	0.30 (0.02, 0.57)
70-90	-0.53 (-2.21, 1.15)	-8.74 (-13.74, -3.75) 0.59	0.16 (-0.27, -0.59)	-0.15 (-0.59, 0.29)
NH <sub>4</sub> <sup>+</sup> , µg/m <sup>3</sup>				
0-9	0.41 (-1.28, 2.09)	2.58 (-1.46, 6.61) 0.05	-0.38 (-0.81, -0.94)	-0.50 (-0.94, -0.05)
10-14	-0.20 (-1.59, 1.18)	4.07 (0.83, 7.31) 0.30	-0.05 (-0.41, 0.30)	-0.01 (-0.37, 0.36)
70-90	-1.59 (-3.89, 0.71)	-5.58 (-11.49, 0.33) 0.53	-0.06 (-0.65, -0.91)	-0.31 (-0.91, 0.30)
NO <sub>3</sub> <sup>-</sup> , µg/m <sup>3</sup>				
0-9	1.22 (-0.92, 3.37)	2.76 (-2.12, 7.63) -0.26	-0.81 (-1.36, -1.61)	-1.04 (-1.61, -0.48)
10-14	-0.31 (-2.03, 1.41)	2.67 (-1.19, 6.52) 0.00	-0.44 (-0.88, 0.00)	-0.47 (-0.92, -0.02)
70-90	-0.92 (-3.55, 1.71)	-9.01 (-15.67, -2.36) 0.28	-0.39 (-1.06, -1.32)	-0.63 (-1.32, 0.06)

Abbreviations: PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter ≤ 2.5 µm; OM, Organic matters; BC, black carbon; SO<sub>4</sub><sup>2-</sup>, sulfate; NO<sub>3</sub><sup>-</sup>, nitrate; NH<sub>4</sub><sup>+</sup>, ammonium; Cl<sup>-</sup>, chloride.

<sup>a</sup> The models was adjusted for age, body mass index, educational levels, ever having fathered a child, daily mean ambient temperature, relative humidity, year and season of semen collection.

<sup>b</sup> Exposure time windows included three key periods of sperm development: epididymal storage (0–9 days before semen collection), sperm motility development (10–14 days before semen collection), spermatogenesis (70–90 days before semen collection).

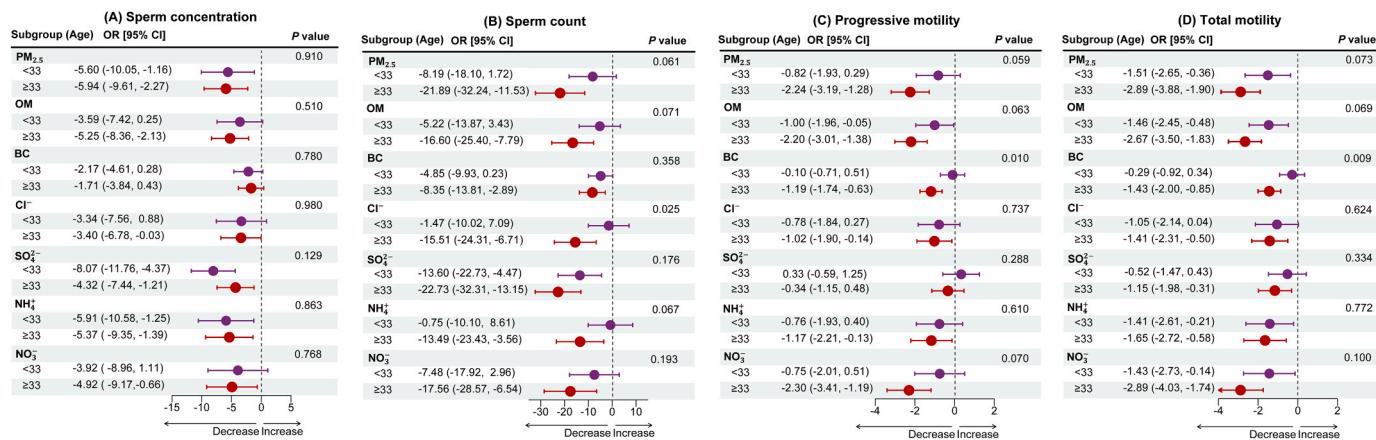
association in a population-based study design. BC and OC primarily originated from combustion sources, such as vehicle emissions, industrial emissions, and biomass burning [10]. Although the biological mechanisms remain unclear, several toxicological studies offer potential explanations for the adverse effects of BC and OM on semen quality [15, 17, 2, 22]. Exposure to BC has been linked with disturbances in DNA methylation, induction of oxidative stress, and systemic inflammation [17, 2, 22]. Recent reviews have linked these biological mechanisms with male reproductive toxicity [28]. For example, Hu et al. reported a significant increase in testicular oxidative stress and inflammation in mice exposed to carbon black nanoparticles, resulting in a rapid decrease in sperm count and sperm motility [13]. Additionally, exposure to BC might disrupt gene expression profiles in spermatozoa, indicating potential genetic mutations that could impact reproductive ability of offspring [15]. Furthermore, our study appears to be the first to establish an association between OM exposure and semen quality. OM mainly originates from mobile and biomass burning sources, and our findings highlight the need for further studies to examine the relationship between OM exposure and semen quality.

Our findings suggested that exposure to Cl<sup>-</sup>, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>, and NO<sub>3</sub><sup>-</sup> was associated with decreased sperm quality. These constituents are primarily formed through atmospheric chemical reactions [10]. Our results were consistent with several epidemiological studies [14, 37]. For example, Wu et al. conducted a study in Guangdong, China, collecting 2314 semen samples from 622 men in 2019. They found that exposure to SO<sub>4</sub><sup>2-</sup> was associated with reduced sperm motility [37]. Similarly, in a cross-sectional study among 1081 men in Wuhan, China, Huang et al. reported that exposure to SO<sub>4</sub><sup>2-</sup> and NH<sub>4</sub><sup>+</sup> was associated with decreased sperm density [14].

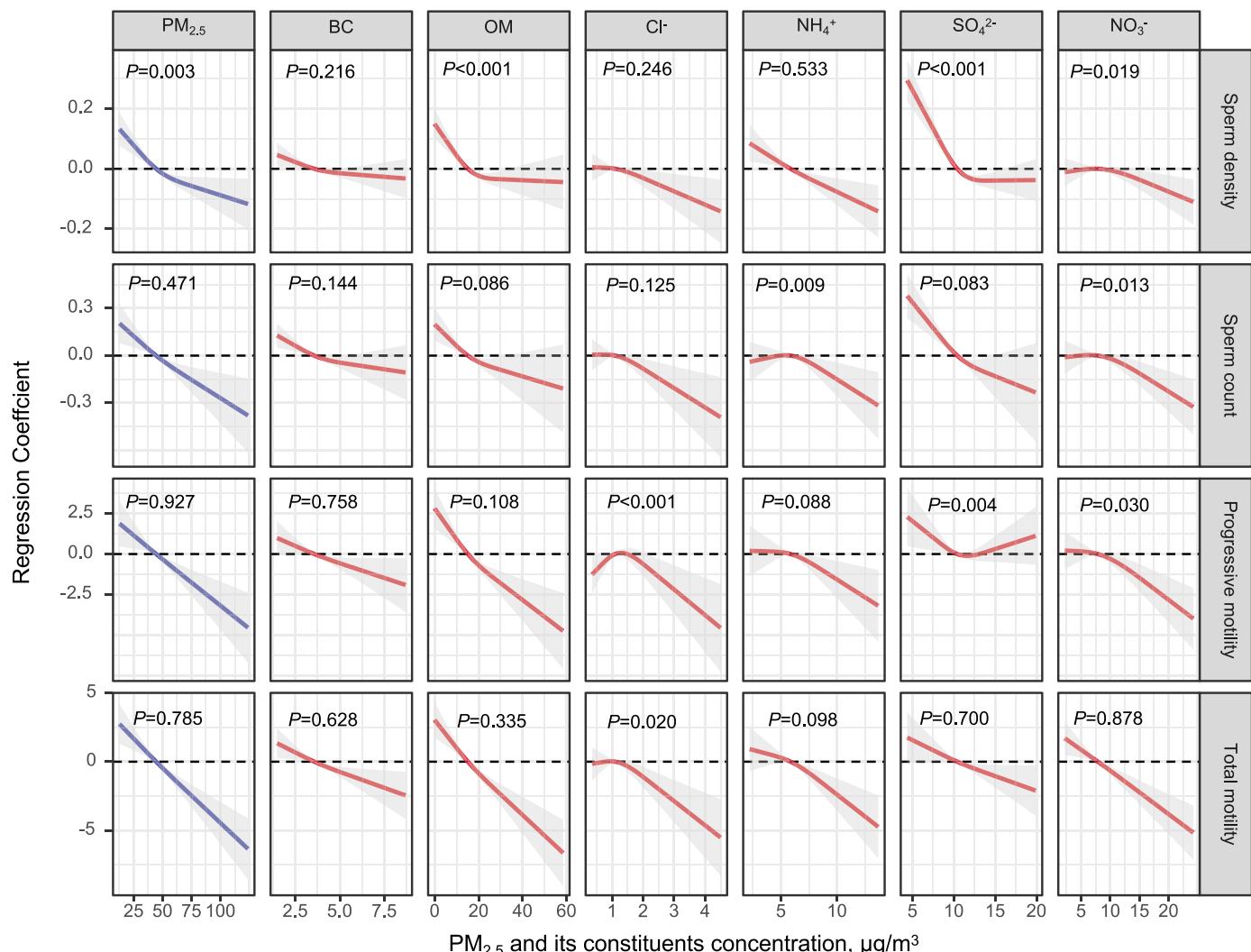
The biological mechanisms underlying the association between PM<sub>2.5</sub> constituents and the reduction in semen quality remain largely unknown, although several potential pathways have been proposed [18, 20, 23]. Exposure to NO<sub>3</sub><sup>-</sup>, SO<sub>4</sub><sup>2-</sup>, and NH<sub>4</sub><sup>+</sup> have been linked to the activation of the hypothalamic-pituitary-adrenal (HPA) axis [23], which can directly inhibit both the hypothalamic-pituitary-gonadal axis and Leydig cell in the testes [20]. This inhibition of the HPA axis might lead to a decrease in testosterone levels, subsequently affecting Sertoli cells and the blood-testis barrier, potentially contributing to spermatogenesis disruption [20]. Additionally, certain constituents of PM<sub>2.5</sub> like NO<sub>3</sub><sup>-</sup>, SO<sub>4</sub><sup>2-</sup>, and NH<sub>4</sub><sup>+</sup> have been linked with inflammatory and coagulation biomarkers. This suggests that PM-induced blood inflammation could play a role in male reproductive impairment [18].

We observed that the association was more pronounced among men aged 33 years and older. One potential explanation for this finding could stem from the longer cumulative exposure durations to environmental factors among older males, coupled with physiological aging, a weakened immune system, and an increased likelihood of chronic conditions [24]. Interestingly, our findings differ from those reported by Zhang and Wu et al. who did not identify a stronger association in older individuals [38, 41].

Our finding of a stronger association among men with a high school education or lower may be partially attributed to differences in awareness, knowledge, lifestyle choices, occupational and residential environments, and healthcare utilization [25]. A study conducted by Jennifer et al. reported that the impact of PM<sub>2.5</sub> was less pronounced



**Fig. 3.** Percent change of sperm quality associated with an interquartile range increase in daily mean concentration of PM<sub>2.5</sub> mass and its constituents stratified by age during the entire sperm development. Models were adjusted for body mass index, educational levels, ever having fathered a child, daily mean ambient temperature, relative humidity, year and season of semen collection. Abbreviations: PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter  $\leq 2.5 \mu\text{m}$ ; OM, organic matters; BC, black carbon; SO<sub>4</sub><sup>2-</sup>, sulfate; NO<sub>3</sub><sup>-</sup>, nitrate; NH<sub>4</sub><sup>+</sup>, ammonium; Cl<sup>-</sup>, chloride.



**Fig. 4.** Exposure-response relationship between PM<sub>2.5</sub> and its constituents and semen quality, with adjustment for body mass index, educational levels, ever having fathered a child, daily mean ambient temperature, relative humidity, year and season of semen collection. Abbreviations: PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter  $\leq 2.5 \mu\text{m}$ ; OM, organic matters; BC, black carbon; SO<sub>4</sub><sup>2-</sup>, sulfate; NO<sub>3</sub><sup>-</sup>, nitrate; NH<sub>4</sub><sup>+</sup>, ammonium; Cl<sup>-</sup>, chloride.

among older individuals with 13 or more years of education, but was more pronounced among those with 8 or fewer years of education [1]. Individuals with higher education levels might be more likely to reside in areas with better environmental quality, thus reducing exposure to air pollution. Additionally, they may also be more likely to pursue occupations associated with less exposure to air pollutants [11].

Our study has several limitations. First, although we controlled for a wide range of potential confounders for the association between PM exposure and semen quality, certain known confounder, such as smoking and alcohol consumption were not available for adjustment in our models. Second, we estimated PM<sub>2.5</sub> constituents from the China High Air Pollutant dataset, which provided data on BC, SO<sub>4</sub><sup>2-</sup>, NO<sub>3</sub><sup>-</sup>, NH<sub>4</sub><sup>+</sup>, Cl<sup>-</sup>, but lacked information on other constituents like Al, Se, Cr, Hg, Mn, Cd, Sb, Tl, Ni, and Pb. In addition, we calculated OM by subtracting the sum of BC, SO<sub>4</sub><sup>2-</sup>, NO<sub>3</sub><sup>-</sup>, NH<sub>4</sub><sup>+</sup>, and Cl<sup>-</sup> concentrations from the PM<sub>2.5</sub> mass concentrations, potentially introducing measurement errors. Thus, cautious interpretation of our findings related to OM is warranted. Third, we estimated PM<sub>2.5</sub> constituent concentration based on participants' geographic locations without considering individual mobility data, which might introduce another source of measurement errors. Fourth, the majority of our participants were located in Wuhan, China, an area characterized by relatively low levels of PM<sub>2.5</sub> and constituents, which could limit the generalizability of our findings to regions with higher PM<sub>2.5</sub> levels.

## 5. Conclusions

Leveraging a large-scale retrospective study involving 27,824 adult men in Hubei, China, we found that exposure to PM<sub>2.5</sub> mass and its constituents, including BC, OM, Cl<sup>-</sup>, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>, and NO<sub>3</sub><sup>-</sup>, was associated with impaired semen quality. We found the association was more pronounced among older individuals and those with lower educational attainment. Given the significant implications of declining sperm quality and the ongoing air pollution, there is a pressing need for further studies to replicate and validate our findings across diverse geographical regions and subpopulations.

## Environmental Implication

Emerging epidemiological studies have investigated the association between PM<sub>2.5</sub> exposure and semen quality, but findings have been mixed. The toxicity of PM<sub>2.5</sub> is primarily driven by its chemical constituents, which vary widely across regions, seasons, and pollution sources. There has been limited study examining the association of PM chemical constituents with semen quality. In our study, we found that among specific constituents, exposure to OM, BC, Cl<sup>-</sup>, or NO<sub>3</sub><sup>-</sup> was associated with a reduction in the sperm total count, sperm density, and progressive and total motility. These findings advance our understanding of the deleterious impact of PM<sub>2.5</sub> on semen quality.

## Source of funding

This study was supported by National Natural Science Foundation of China (82373535).

## CRediT authorship contribution statement

**Zhang Yangchang:** Conceptualization, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft.  
**Wei Jing:** Data curation, Investigation, Methodology, Resources, Writing – review & editing.  
**Zhao Shi:** Conceptualization, Validation, Writing – review & editing.  
**Zeng Qiang:** Conceptualization, Resources, Supervision, Writing – review & editing.  
**Sun Shengzhi:** Conceptualization, Funding acquisition, Resources, Supervision, Writing – review & editing.  
**Cao Wangnan:** Conceptualization, Investigation, Resources, Supervision, Validation, Writing – review & editing.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data Availability

Data will be made available on request.

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2023.133313.

## References

- [1] Ailshire, J., Walsemann, K.M., 2011. Education differences in the adverse impact of PM<sub>2.5</sub> on incident cognitive impairment among U.S. older adults. *J Alzheimers Dis* 79, 615–625. <https://doi.org/10.3233/jad-200765>.
- [2] Baccarelli, A., Wright, R.O., Bollati, V., et al., 2009. Rapid DNA methylation changes after exposure to traffic particles. *Am J Respir Crit Care Med* 179, 572–578. <https://doi.org/10.1164/ajrccm.180.101030>.
- [3] Beelen, R., Raaschou-Nielsen, O., Stafoggia, M., et al., 2014. Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. *Lancet* 383, 785–795. [https://doi.org/10.1016/s0140-6736\(13\)62158-3](https://doi.org/10.1016/s0140-6736(13)62158-3).
- [4] Benjamini, Y., Hochberg, Y., 2018. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc: Ser B (Methodol)* 57, 289–300. <https://doi.org/10.1111/j.2517-6161.1995.tb02031.x>.
- [5] Cai, X., Ni, H., Wang, Q., et al., 2023. Sperm quality decline associated with gaseous pollutant exposure: evidence from a large cohort multicenter study. *J Hazard Mater* 460, 132330. <https://doi.org/10.1016/j.jhazmat.2023.132330>.
- [6] Cheng, Y., Tang, Q., Lu, Y., et al., 2022. Semen quality and sperm DNA methylation in relation to long-term exposure to air pollution in fertile men: a cross-sectional study. *Environ Pollut* 300, 118994. <https://doi.org/10.1016/j.envpol.2022.118994>.
- [7] Dai, X., Chen, G., Zhang, M., et al., 2023. Exposure to ambient particulate matter affects semen quality: a case study in Wenzhou, China. *Andrology* 11, 444–455. <https://doi.org/10.1111/andr.13326>.
- [8] de Mesnard, L., 2013. Pollution models and inverse distance weighting: some critical remarks. *Comput Geosci* 52, 459–469. <https://doi.org/10.1016/j.cageo.2012.11.002>.
- [9] Fainberg, J., Kashanian, J.A., 2019. Recent advances in understanding and managing male infertility. *F1000Res* 16 8. <https://doi.org/10.12688/f1000research.170761.1>.
- [10] Fong, K.C., Di, Q., Kloog, I., et al., 2019. Relative toxicities of major particulate matter constituents on birthweight in Massachusetts. *Environ Epidemiol* 3, e047. <https://doi.org/10.1097/ee9.0000000000000047>.
- [11] Garcia-Mayor, J., Moreno-Llamas, A., la Cruz-Sanchez, E., et al., 2021. High educational attainment redresses the effect of occupational social class on health-related lifestyle: findings from four Spanish national health surveys. *Ann Epidemiol* 58, 29–37. <https://doi.org/10.1016/j.annepidem.2021.02.010>.
- [12] Gutierrez-Avila, I., Riojas-Rodriguez, H., Colicino, E., et al., 2023. Short-term exposure to PM<sub>2.5</sub> and 1.5 million deaths: a time-stratified case-crossover analysis in the Mexico City Metropolitan Area. *Environ Health* 22, 70. <https://doi.org/10.1186/s12940-023-01024-4>.
- [13] Hu, Z., Zhang, Y., Zhang, L., et al., 2021. Respiratory exposure to carbon black nanoparticles may induce testicular structure damage and lead to decreased sperm quality in mice. *Reprod Toxicol* 106, 32–41. <https://doi.org/10.1016/j.reprotox.2021.10.001>.
- [14] Huang, X., Zhang, B., Wu, L., et al., 2019. Association of exposure to ambient fine particulate matter constituents with semen quality among men attending a fertility center in China. *Environ Sci Technol* 53, 5957–5965. <https://doi.org/10.1021/acs.est.8b06942>.
- [15] Jiang, S., Chen, L., Shen, J., et al., 2023. Adverse effects of prenatal exposure to oxidized black carbon particles on the reproductive system of male mice. *Toxicol* 2023 11. <https://doi.org/10.3390/toxicols11070556>.
- [16] Levine, H., Jorgensen, N., Martino-Andrade, A., et al., 2023. Temporal trends in sperm count: a systematic review and meta-regression analysis of samples collected globally in the 20th and 21st centuries. *Hum Reprod Update* 29, 157–176. <https://doi.org/10.1093/humupd/dmac035>.
- [17] Li, W., Dorans, K.S., Wilker, E.H., et al., 2017. Short-term exposure to ambient air pollution and biomarkers of systemic inflammation: the framingham heart study. *Arterioscler Thromb Vasc Biol* 37, 1793–1800. <https://doi.org/10.1161/ATVBAHA.117.309799>.
- [18] Liu, C., Cai, J., Qiao, L., et al., 2017. The acute effects of fine particulate matter constituents on blood inflammation and coagulation. *Environ Sci Technol* 51, 8128–8137. <https://doi.org/10.1021/acs.est.7b00312>.

- [19] Liu, J., Dai, Y., Li, R., Yuan, J., Wang, Q., Wang, L., 2023. Does air pollution exposure affect semen quality? Evidence from a systematic review and meta-analysis of 93,996 Chinese men. *Front Public Health* 11, 1219340.
- [20] Nargund, V.H., 2015. Effects of psychological stress on male fertility. *Nat Rev Urol* 12, 373–382. <https://doi.org/10.1038/nrurol.2015.112>.
- [21] Nassan, F.L., Wang, C., Kelly, R.S., et al., 2021. Ambient PM<sub>2.5</sub> species and ultrafine particle exposure and their differential metabolic signatures. *Environ Int* 151, 106447. <https://doi.org/10.1016/j.envint.2021.106447>.
- [22] Niranjani, R., Thakur, A.K., et al., 2017. The toxicological mechanisms of environmental soot (black carbon) and carbon black: focus on oxidative stress and inflammatory pathways. *Front Immunol* 8, 763. <https://doi.org/10.3389/fimmu.2017.00763>.
- [23] Niu, Y., Chen, R., Xia, Y., et al., 2018. Fine particulate matter constituents and stress hormones in the hypothalamus-pituitary-adrenal axis. *Environ Int* 119, 186–192. <https://doi.org/10.1016/j.envint.2018.06.027>.
- [24] Pun, V.C., Kazemiparkouhi, F., Manjourides, J., et al., 2017. Long-Term PM<sub>2.5</sub> exposure and respiratory, cancer, and cardiovascular mortality in older US adults. *Am J Epidemiol* 186, 961–969. <https://doi.org/10.1093/aje/kwx166>.
- [25] Raghupathi, V., Raghupathi, W., 2020. The influence of education on health: an empirical assessment of OECD countries for the period 1995–2015. *Arch Public Health* 78, 20. <https://doi.org/10.1186/s13690-020-00402-5>.
- [26] Shang, Y., Zhu, T., Lenz, A.G., et al., 2013. Reduced in vitro toxicity of fine particulate matter collected during the 2008 Summer Olympic Games in Beijing: the roles of chemical and biological components. *Toxicol Vitr* 27, 2084–2093. <https://doi.org/10.1016/j.tiv.2013.08.004>.
- [27] Sun, S., Zhao, J., Cao, W., et al., 2020. Identifying critical exposure windows for ambient air pollution and semen quality in Chinese men. *Environ Res* 189, 109894.
- [28] Wang, L., Luo, D., Liu, X., et al., 2021. Effects of PM<sub>2.5</sub> exposure on reproductive system and its mechanisms. *Chemosphere* 264, 128436. <https://doi.org/10.1016/j.chemosphere.2020.128436>.
- [29] Wang, L., Xu, T., Wang, Q., et al., 2023. Exposure to fine particulate matter constituents and human semen quality decline: a multicenter study. *Environ Sci Technol* 57, 13025–13035.
- [30] Wang, Y.X., You, L., Zeng, Q., et al., 2015. Phthalate exposure and human semen quality: Results from an infertility clinic in China. *Environ Res* 142, 1–9. <https://doi.org/10.1016/j.acs.est.3c03928>.
- [31] Wei, J., Li, Z., Cribb, M., et al., 2020. Improved 1km resolution PM<sub>2.5</sub> estimates across China using enhanced space-time extremely randomized trees. *Atmos Chem Phys* 20, 3273–3289. <https://doi.org/10.5194/acp-20-3273-2020>.
- [32] Wei, J., Li, Z., Lyapustin, A., et al., 2021. Reconstructing 1-km-resolution high-quality PM<sub>2.5</sub> data records from 2000 to 2018 in China: spatiotemporal variations and policy implications. *Remote Sens Environ* 252, 112136. <https://doi.org/10.1016/j.rse.2020.112136>.
- [33] Wei, J., Li, Z., Chen, X., et al., 2023. Separating daily 1 km PM<sub>2.5</sub> inorganic chemical composition in China since 2000 via deep learning integrating ground, satellite, and model data. *Environ Sci Technol* 2023. <https://doi.org/10.1021/acs.est.3c00272>.
- [34] Wei, J., Wang, J., Li, Z., Kondragunta, S., Anenberg, S., Wang, Y., et al., 2023. Long-term mortality burden trends attributed to black carbon and PM<sub>2.5</sub> from wildfire emissions across the continental USA from 2000 to 2020: a deep learning modelling study. *Lancet Planet Health* (7), e963–e975. [https://doi.org/10.1016/S2542-5196\(23\)00235-8](https://doi.org/10.1016/S2542-5196(23)00235-8).
- [35] World Health Organization, 2010. WHO laboratory manual for the examination and processing of human semen. World Health Organization, Geneva.
- [36] Wu, C., Zhang, Y., Wei, J., et al., 2022. Associations of early-life exposure to submicron particulate matter with childhood asthma and wheeze in China. *JAMA Netw Open* 5, e2236003. <https://doi.org/10.1001/jamanetworkopen.2022.36003>.
- [37] Wu, H., Yu, X., Wang, Q., et al., 2021. Beyond the mean: quantile regression to differentiate the distributional effects of ambient PM<sub>2.5</sub> constituents on sperm quality among men. *Chemosphere* 285, 131496. <https://doi.org/10.1016/j.chemosphere.2021.131496>.
- [38] Wu, W., Chen, Y., Cheng, Y., et al., 2022. Association between ambient particulate matter exposure and semen quality in fertile men. *Environ Health* 21, 16. <https://doi.org/10.1186/s12940-022-00831-5>.
- [39] Xu, R., Zhong, Y., Li, R., 2023. Association between exposure to ambient air pollution and semen quality: a systematic review and meta-analysis. *Sci Total Environ* 870, 161892. <https://doi.org/10.1016/j.scitotenv.2023.161892>.
- [40] Zeng, Q., Wang, Y.X., Xie, S.H., 2014. Drinking-water disinfection by-products and semen quality: a cross-sectional study in China. *Environ Health Perspect* 122, 741–746. <https://doi.org/10.1289/ehp.1307067>.
- [41] Zhang, Y., Wei, J., Liu, C., et al., 2023. Association between ambient PM<sub>1</sub> and semen quality: a cross-sectional study of 27,854 men in China. *Environ Int* 175, 107919. <https://doi.org/10.1016/j.envint.2023.107919>.
- [42] Zhao, Y., Zhu, Q., Lin, J., et al., 2022. Association of exposure to particulate matter air pollution with semen quality among men in China. *JAMA Netw Open* 5, e2148684. <https://doi.org/10.1001/jamanetworkopen.2021.48684>.