



# Individual and joint associations of air pollutants exposure with semen quality: A retrospective longitudinal study in Wenzhou, China

Xuchao Dai<sup>1</sup> · Guangyuan Liu<sup>2</sup> · Chengshuang Pan<sup>3</sup> · Feidi Li<sup>2</sup> · Yawen Liu<sup>2</sup> · Jiaxin Liu<sup>2</sup> · Gang Chen<sup>4</sup> · Mengqi Zhang<sup>5</sup> · Qianjin Fei<sup>3</sup> · Jiujia Zheng<sup>3</sup> · Hong Huang<sup>2,6</sup> · Zhigang Wu<sup>7,8</sup>

Received: 17 April 2024 / Accepted: 17 July 2024

© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2024

## Abstract

**Purpose** The impact of air pollution on semen quality has been confirmed, yet the joint effect remains unclear. We evaluate the individual and joint associations of particulate (PM<sub>2.5</sub> and PM<sub>10</sub>) and gaseous pollutants (NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub> and CO) with semen quality.

**Methods** We included 5,114 men in this study from 2014 to 2022. The individual and joint associations were measured by multiple linear regression models.

**Results** Sperm motility and semen volume were inversely associated with pollutant concentrations during every stage of sperm development, especially at lag days 0–9 and 10–14 (all  $P < 0.05$ ). Stratified analyses showed that the study pollutants (except CO) had a positive effect on semen concentration during the stage of sperm development, especially in spring and autumn, while a decreased total sperm number was associated with CO (all  $P < 0.05$ ). However, joint associations of particulate and gaseous pollutants with semen quality parameters were not statistically significant (all  $P > 0.05$ ).

**Conclusions** During all stages of sperm development, particulate and gaseous pollutants had individual negative impacts on sperm motility and semen volume, and these impacts were less pronounced in spring and autumn. Our findings highlight the importance and necessity of reducing the exposure to pollutants especially in the critical stage of sperm development to improve semen quality.

**Keywords** Air pollution · Semen quality · Susceptible periods · Male reproductive health · Exposure–response relation

## Abbreviations

ARIMA Autoregressive Integrated Moving Average model  
BMI Body mass index

CASA Computer-assisted sperm analysis  
CI Confidence interval  
CO Carbon monoxide  
IQR Interquartile ranges  
IL6 Interleukin-6  
IVF In vitro fertilization

Xuchao Dai and Guangyuan Liu contributed equally to this work.

✉ Hong Huang  
huanghongpanda@163.com

✉ Zhigang Wu  
andrologywzg@wmu.edu.cn

<sup>1</sup> The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China

<sup>2</sup> School of Public Health, Wenzhou Medical University, Zhejiang Province, Wenzhou 325035, China

<sup>3</sup> Reproductive Medicine Center, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, China

<sup>4</sup> Hospital Infection Control Management Department, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou 325027, China

<sup>5</sup> School and Hospital of Stomatology, Wenzhou Medical University, Wenzhou 325027, China

<sup>6</sup> Zhejiang Provincial Key Laboratory of Watershed Sciences and Health, Wenzhou 325035, China

<sup>7</sup> Department of Urology, The First Affiliated Hospital of Wenzhou Medical University, Zhejiang Province, Wenzhou 325000, China

<sup>8</sup> The Quzhou Affiliated Hospital of Wenzhou Medical University, Quzhou People's Hospital, Quzhou 324000, China

TNF-a	Tumor necrosis factor-a
5-hmC	5-Hydroxymethylcytosine
ESR1	Estrogen receptor 1 Gene
NO <sub>2</sub>	Nitrogen dioxide
O <sub>3</sub>	Ozone
PM	Particulate matter
PM <sub>2.5</sub>	Particulate matter with diameter less than 2.5 μm
PM <sub>10</sub>	Particulate matter with diameter less than 10 μm
RCS	Restricted cubic splines model
ROS	Reactive oxygen species
Seadec	Seasonally Decomposed Imputation
SO <sub>2</sub>	Sulfur dioxide
WHO	World Health Organization

## Introduction

Air pollution is increasing as society develops, which is a major challenge for human health (Sicard et al. 2023). A review study reported strong associations between air pollutants and male semen quality, but these findings remain controversial (Xu et al. 2023). For instance, Yang et al. reported that exposure to PM<sub>2.5</sub>, PM<sub>10</sub>, and SO<sub>2</sub> was positively associated with sperm motility, while exposure to O<sub>3</sub> was negatively associated with sperm motility (Yang et al. 2021). In contrast, Qiu et al. discovered that exposure to PM<sub>10</sub>, PM<sub>2.5</sub> and CO was associated with decreased sperm concentration and progressive motility, while O<sub>3</sub> positively associated with sperm progressive motility (Qiu et al. 2020). In addition, related studies have focused on assessing the influence of single kinds of pollutants on semen quality by using single-pollutant models (Lu et al. 2023; Huang et al. 2020; Wu et al. 2022), while evidence on the impacts of simultaneous exposure to different kinds of pollutants on semen quality is scarce (Zhang et al. 2023a). Air pollutants can be categorized as particulate pollutants or gaseous pollutants. Since particulate and gaseous pollutants have similar biological mechanisms for health, such as oxidative stress, endothelial dysfunction, and macrophage dysfunction (Gangwar et al. 2020; Olesiejuk and Chalubinski 2023; Watanabe and Oonuki 1999), we hypothesize that co-exposure to these pollutants may result in more severe damage to semen quality.

Human spermatogenesis takes approximately 90 days, and the time period is usually divided into three key stages: (1) sperm storage in the epididymis (0–9 days before ejaculation), (2) sperm motility development (10–14 days before ejaculation), and (3) spermatogenesis (70–90 days before ejaculation), respectively (Sokol et al. 2006). Identifying the influence of pollutant exposure on semen quality is highly important for developing precise interventions to improve male reproductive health, but most current studies

have focused on the three critical periods mentioned above (Huang et al. 2020; Zhou et al. 2014; Ma et al. 2022), while a few studies have considered the effect of this approach beyond the three critical periods (15–69 days before ejaculation) (Yang et al. 2021; Wu et al. 2022). Failing to consider the association of periods of discontinuity may lead to biased assessment results and the identification of erroneous exposure periods (Sun et al. 2020).

Based on the existing knowledge, we conducted a retrospective longitudinal study to define the potential individual and joint impacts of different kinds of air pollutants on semen quality. The aim of this paper is to (1) evaluate the individual and joint associations of particulate and gaseous pollutants with semen quality, (2) further identify associations in five exposure periods (0–9, 10–14, 15–69, 70–90, and 0–90 days before ejaculation) to ensure continuity, and (3) explore whether the associations differ by age and season and find the best age and season for semen quality.

## Material and methods

### Participants

Participants were from the Reproductive Medicine Center of the First Affiliated Hospital of Wenzhou Medical University in Wenzhou, China. Wenzhou is a highly developed economic region on the eastern coast of China, that is situated between 119°37'–121°18' east longitude and 27°03'–28°36' north latitude, and has a permanent population of approximately 9.7 million. Due to the limited availability of data on particulate matter and gaseous pollutants (Dai et al. 2023), we chose to conduct our study within the time frame of May 13, 2014 to December 31, 2022, and focused on the main urban area (Lucheng District, Ouhai District, and Longwan District). A total of 63,680 men underwent semen examination for physical examination or fertility in this hospital during 2014–2022. The exclusion criteria selection for our participants were as follows: (1) the participants was not located in the urban area of Wenzhou, (2) the testing time did not fall within the study period, (3) the records were incomplete and (4) participants had a reproductive condition that may have affected semen quality. A total of 5,114 participants were ultimately recruited as study participants. Fig. S1 illustrates the specific process of screening the research subjects.

### Semen analysis

Participants could only be examined by providing a semen sample by masturbating in the collection room after 2–7 days of abstinence. The semen quality parameters were detected and analyzed by a computer-assisted sperm analysis (CASA) system (MICROPTIC S. L. Company, Viladomat,

Barcelona, Spain). The specific semen analysis procedures and laboratory quality control procedures used were described in detail in our previous study (Dai et al. 2023). In accordance with World Health Organization (WHO) guidelines (World Health Organization 2010), five semen quality parameters, progressive motility (%), total motility (%), sperm concentration ( $10^6/\text{ml}$ ), total sperm number ( $10^6$ ) and semen volume (ml) were taken into account.

### Air pollution exposure assessment

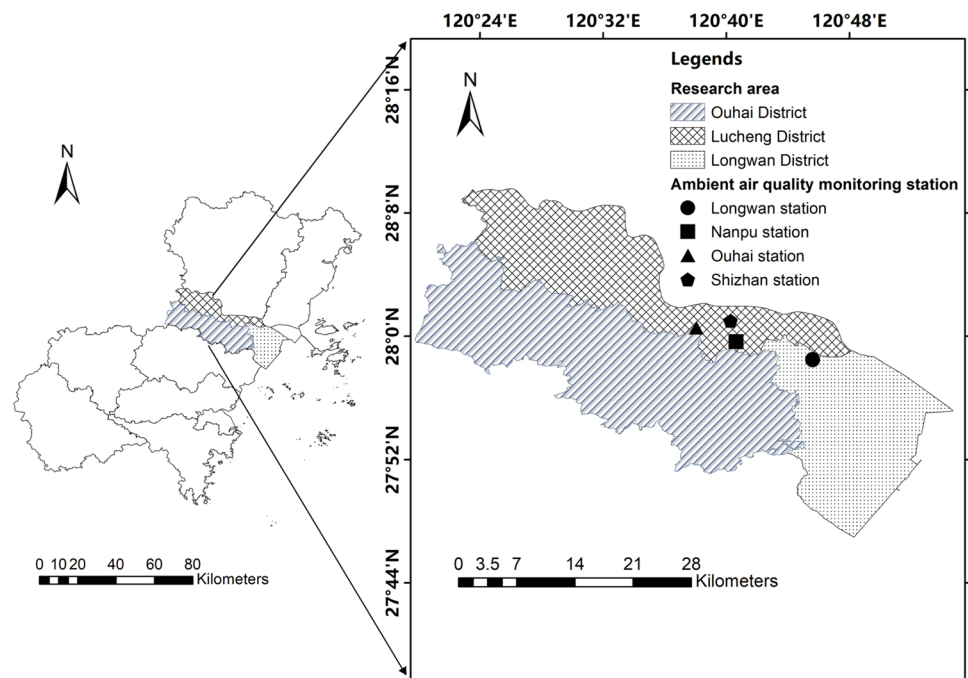
Daily monitoring data on  $\text{PM}_{2.5}$  ( $\mu\text{g}/\text{m}^3$ ),  $\text{PM}_{10}$  ( $\mu\text{g}/\text{m}^3$ ),  $\text{SO}_2$  ( $\mu\text{g}/\text{m}^3$ ),  $\text{NO}_2$  ( $\mu\text{g}/\text{m}^3$ ), the 8-h average of  $\text{O}_3$  ( $\mu\text{g}/\text{m}^3$ ), and  $\text{CO}$  ( $\text{mg}/\text{m}^3$ ) were obtained from the official website of the environmental protection department (<https://air.cnemc.cn:18007/>) during the study time period, and there were four air quality monitoring stations in the study area (Fig. 1). Since we were unable to obtain accurate address data for the study participants due to privacy participants, we utilized daily monitoring concentration data from the vicinity of their registered home address to represent participants' daily exposure level. Specifically, the concentration at the monitoring station in each district represents the level of exposure in that area, while the exposure concentration in Lucheng District is calculated based on the average value of the Shizhan station and the Nanpu monitoring station. Pollutant data from the four stations were missing for a total of 22 days. Based on the research conducted by Priti K. et al. (Priti K et al. 2023), we examined six different univariate time series imputation methods (mean, median, last observation carried forward, spline, Kalman smoothing and

seasonally decomposed) using the “impute TS” package in R and assessed the accuracy of these estimation methods by five indicators (Supplement 1 and 2). After comparing the performance, accuracy and authenticity of the imputation methods, we selected the imputed data using the state space representation of univariate autoregressive integrated moving average model (ARIMA) and Kalman smoothing function for subsequent analysis (Table S1 and Fig. S3-S6). For each research participant, we calculated their average exposure to air pollution during the entire period (lag 0–90 days) and four crucial periods (lag 0–9, 10–14, 15–69 and 70–90 days).

### Covariates

All information on the subjects was collected by trained physicians and recorded in the hospital information management system, including age (continuous), occupation (categorical), educational level (categorical), alcohol consumption (categorical: yes, no), smoking (categorical: yes, no), abstinence days (continuous), ever having fathered a child (categorical: yes, no), and collection date. Based on previous study (Zhang et al. 2023b), participants without age, occupation, or educational level information were classified as “Unknown”. Specifically, these reclassified variables include: age (categorized into  $\leq 30$ , 31–39,  $\geq 40$  years, unknown), education level (categorized into college and high, high school, middle school and lower, unknown), occupation (categorized into worker, businessman, peasant, intellectual, others, unknown) and abstinence periods (categorized into 2–3, 4–5 and 6–7 days). The season of sperm

**Fig. 1** Spatial distribution of the study area ( $n=3$ ) and ambient air quality monitoring station ( $n=4$ )



collection was group as spring, summer, autumn and winter according to the date of semen examination. The average daily temperature and average daily relative humidity were calculated for meteorological conditions and were obtained from the China Meteorological Data Sharing System (<http://data.cma.cn/>). Moreover, we filled in the 2-day missing meteorological data using the same methods used for air pollutants.

## Statistical analyses

Descriptive statistics were summarized as frequency and percentage for categorical variable and median and interquartile range (IQR) for continuous variable with skewed distribution. Spearman's correlation coefficient was employed to investigate the correlations between air pollutants due to their skewed distribution. In addition, we employed a Box-Cox transformation method to ensure that the semen quality parameters were normally or nearly normally distributed (Supplement 3).

To avoid collinearity between pollutants, we used multiple linear regression through single-pollutant model to examine the relationship between individual exposure to each air pollutant (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub> and CO) and semen parameters (progressive motility, total motility, sperm concentration, total sperm number and semen volume) during lag 0–90 days. All models were adjusted by age, ever having fathered a child, smoking, alcohol consumption, education, occupation, abstinence periods, season of sperm collection, average daily ambient temperature during lag 0–90 days and mean relative humidity during lag 0–90 days. We calculated the regression coefficients ( $\beta$ ) and 95% confidence intervals (CIs) for each semen parameter associated with each IQR increase in air pollution exposures. Furthermore, air pollutant exposure was divided into quintiles and regression coefficients were estimated using the first quintile as the reference level. We performed tests for linear trend by entering the median value of each air pollutant as a continuous variable in the models.

To further investigate the exposure–response relationship between air pollutants and semen parameters, we utilized a restricted cubic spline with four knots located at the 5th, 35th, 65th, and 95th percentiles of the distribution of each pollutant's exposure level in the model. An analysis of variance (ANOVA) was used to assess deviations from linearity in the exposure–response curve.

Besides showing associations throughout the entire sperm development period (lag 0–90 days), we also constructed different exposure models with four critical windows (lag 0–9, 10–14, 15–69 and 70–90 days) to further evaluate the relationship between exposure to each pollutant and semen quality and identified sensitivity windows. Ultimately, after comprehensively analyzing the independent effects of each

air pollutant on semen quality parameters, we added a multiplicative interaction term to the multiple linear regression model to assess whether the effect of particulate matter mass concentration on semen parameters changes at different levels of gaseous pollutants. The statistical model used can be represented as follows:

$$Y_i = \beta_0 + \beta_1 X_{i1} + \beta_2 X_{i2} + \beta_3 (X_{i1} \times X_{i2}) + \epsilon_i$$

where  $Y_i$  represents the semen parameter of interest for individual  $i$ ,  $X_{i1}$  is the level of particulate matter exposure for individual  $i$ ,  $X_{i2}$  is the level of gaseous pollutants exposure for individual  $i$ ,  $\beta_0$  is the intercept,  $\beta_1$  and  $\beta_2$  are the coefficients for the main effects of particulate matter and gaseous pollutants, respectively,  $\beta_3$  is the coefficient for the interaction term, which quantifies how much the effect of one variable change when the other variable is present,  $\epsilon_i$  is the error term for individual.

The  $P$ -value returned for the  $\beta_3$  estimate corresponds to the interaction effect between semen parameters and air pollution value.

We performed a stratified study by age ( $\leq 30$ , 31–39, and  $\geq 40$  years) and season (spring, summer, autumn, and winter) to explore its potential effect modification on the association of air pollution exposure with semen quality. In addition, we conducted sensitivity analysis to assess the robustness of our findings. First, we restricted the data to the complete record only (delete 636 incomplete records). Second, to verify whether the relationship could still be found for healthy participants, we repeated the main analyses in a subgroup ( $n = 3,660$ ) that excluded subjects with abnormal sperm concentrations ( $< 15 \times 10^6$  /mL), total sperm number ( $< 39 \times 10^6$ ), total motility ( $< 40\%$ ), progressive motility ( $< 32\%$ ) or semen volume ( $< 1.5$  mL) according to WHO referenced values (World Health Organization 2010). All the statistical analyses were performed using R (version 4.3.2). All  $P$ -values were two-sided, and  $P < 0.05$  was considered statistically significant.

## Results

### Population characteristics, semen parameters and environmental exposure

Table 1 presents the characteristics of men and semen quality parameter with overall ( $n = 5,114$ ) and normal semen quality ( $n = 3,660$ ). The participants were predominantly 30–39 years old (55.4%), worker (73.2%) and had an education level of middle school and lower (38.9%). More than half of the participants had never had fathered a child (62%), had never smoker (99%) or had never drunk alcohol (93.4%). The median (IQR) values of sperm progressive motility,



**Table 1** Basic characteristics of all participants and the normal semen quality group

Characteristic	All participants (n=5114)	Normal semen quality group (n=3660) <sup>a</sup>
Age, years, n (%)		
≤30	1617 (31.6)	1192 (32.6)
31–39	2831 (55.4)	2031 (55.5)
≥40	655 (12.8)	431 (11.8)
Unknown	11 (0.2)	6 (0.2)
Ever having fathered a child, n (%)		
Yes	1945 (38.0)	1424 (38.9)
No	3169 (62.0)	2236 (61.1)
Alcohol consumption, n (%)		
Yes	52 (1.0)	36 (1.0)
No	5062 (99.0)	3624 (99.0)
Smoking, n (%)		
Yes	335 (6.6)	247 (6.7)
No	4779 (93.4)	3413 (93.3)
Occupation, n (%)		
Worker	3742 (73.2)	2657 (72.6)
Businessman	486 (9.5)	370 (10.1)
Peasant	41 (0.8)	27 (0.7)
Intellectual	327 (6.4)	235 (6.4)
Others	404 (7.9)	292 (8.0)
Unknown	114 (2.2)	79 (2.2)
Education, n (%)		
College and higher	1791 (35.0)	1329 (36.3)
High school	747 (14.6)	517 (14.1)
Middle school and lower	1988 (38.9)	1415 (38.7)
Unknown	588 (11.5)	399 (10.9)
Abstinence periods, day, n (%)		
2–3	1635 (32.0)	1169 (31.9)
4–5	2565 (50.2)	1872 (51.1)
6–7	914 (17.9)	619 (16.9)
Season, n (%)		
Spring (Mar-May)	1412 (27.6)	1030 (28.1)
Summer (Jun-Aug)	1399 (27.4)	987 (27.0)
Autumn (Sep-Nov)	1277 (25.0)	923 (25.2)
Winter (Dec-Feb)	1026 (20.1)	720 (19.7)
Progressive motility, % <sup>b</sup>	55.3 (28.0)	61.8 (21.8)
Total motility, % <sup>b</sup>	63.3 (26.4)	69.4 (20.5)
Sperm concentration, × 10 <sup>6</sup> /ml <sup>b</sup>	72.5 (86.8)	86.1 (82.7)
Total sperm number, × 10 <sup>6</sup> <sup>b</sup>	221.6 (277.6)	276.8 (279.7)
Semen volume, ml <sup>b</sup>	3.2 (1.9)	3.3 (1.9)

Data were given as n (percent) or median (IQR) as indicated. Column percentages may not add up to 100 due to rounding

<sup>a</sup>Group defined by semen volume ≥ 1.5 ml, progressive motility ≥ 32%, total motility ≥ 32%, sperm concentration ≥ 15 × 10<sup>6</sup>/ml and total sperm number ≥ 39 × 10<sup>6</sup>/sample. <sup>b</sup>Data were given as median (IQR)

sperm total motility, sperm concentration, total sperm number and semen volume for all participants were 55.3% (28%), 63.3% (26.4%), 72.5 (86.8) × 10<sup>6</sup>/ml, 221.6 (277.6) × 10<sup>6</sup> per sample and 3.2 (1.9) ml, respectively.

Table S1 presents the comparative outcomes of the six interpolation techniques. The mean interpolation's precision proves inferior to that of the median approach. Since the distribution of CO exposure lacks a discernible seasonal pattern, the seasonal decomposition imputation (seadec) method was deemed unsuitable. Consequently, we narrowed our focus to comparing four methodologies – median, spline, Kalman, and seadec – which demonstrated comparable performance levels (Fig. S3-S6). Spline interpolation frequently exhibited the optimal goodness of fit and accuracy; however, this came at the expense of compromising the authenticity of interpolated data points (values of imputed data < 0). Additionally, the median interpolation neglects vital temporal trend details. Balancing these considerations, Kalman smoothing emerges as a preferred solution, effectively capturing time-dependent features such as trends, seasonality, and cyclical patterns with high accuracy.

Table 2 illustrates the distribution for air pollutants at each station, relative humidity and temperature in the three districts. Among the three districts within the study period, the highest concentrations of SO<sub>2</sub> (7.690 μg/m<sup>3</sup>) and O<sub>3</sub> (67.750 μg/m<sup>3</sup>) were found in Lucheng District; the highest concentrations of PM<sub>2.5</sub> (30.580 μg/m<sup>3</sup>) and CO (0.690 mg/m<sup>3</sup>) were found in Ouhai District; and the highest concentrations of PM<sub>10</sub> (55.000 μg/m<sup>3</sup>) and NO<sub>2</sub> (39.170 μg/m<sup>3</sup>) were found in Longwan District. Spearman's correlation coefficients between air pollutants other than O<sub>3</sub> were usually intermediate to high (r > 0.5) (Fig. S2).

### Air pollutants and semen parameters

The associations of air pollutants with semen quality during the 0–90 days before ejaculation for the entire group are shown in Table 3. Air pollutants were significantly negatively associated with sperm progressive motility, total motility and semen volume in the entire group (all *P* < 0.05) (Table 3), and there was a clear linear trend when air pollutant levels were considered as quintiles (*P*<sub>line trend</sub> < 0.05). In addition, there was a negative association between CO exposure and total sperm number. On the contrary, the results of several models suggest that some air pollutants (such as PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> and O<sub>3</sub>) may be significantly positively associated with sperm concentration or total sperm number (all *P* < 0.05). Table S2 shows the joint association of particulate matter with gaseous pollutants on semen parameters in the entire group, and the results showed no interaction (all *P*<sub>interactions</sub> > 0.05).

Figure 2 presents the exposure–response curves for air pollutants and semen parameters using a restricted cubic

**Table 2** Environmental exposure data between May 20, 2014 and December 26, 2022 in the three study sites

Pollutant	Lucheng District	Ouhai District	Longwan District
PM <sub>2.5</sub> (µg/m <sup>3</sup> )			
Station 1	28.920 (22.935)	30.580 (22.165)	26.870 (20.020)
Station 2	28.380 (21.085)		
Average	28.730 (21.845)		
PM <sub>10</sub> (µg/m <sup>3</sup> )			
Station 1	53.120 (38.640)	52.7500 (36.600)	55.000 (37.200)
Station 2	51.360 (33.960)		
Average	52.460 (35.763)		
SO <sub>2</sub> (µg/m <sup>3</sup> )			
Station 1	7.460 (6.074)	7.500 (6.000)	7.380 (5.625)
Station 2	7.960 (6.153)		
Average	7.690 (6.145)		
NO <sub>2</sub> (µg/m <sup>3</sup> )			
Station 1	31.710 (22.170)	37.250 (22.050)	39.170 (24.125)
Station 2	30.620 (18.810)		
Average	31.185 (20.155)		
O <sub>3</sub> (µg/m <sup>3</sup> )			
Station 1	67.500 (42.745)	62.750 (40.675)	60.500 (43.325)
Station 2	67.750 (41.490)		
Average	67.750 (41.045)		
CO (mg/m <sup>3</sup> )			
Station 1	0.700 (0.410)	0.690 (0.340)	0.630 (0.300)
Station 2	0.630 (0.300)		
Average	0.660 (0.335)		
Relative humidity	78.000 (17.500)	78.000 (17.500)	78.000 (17.500)
Temperature (°C)	20.300 (12.800)	20.300 (12.800)	20.300 (12.800)

Data were given as median (IQR) as indicated. IQR: interquartile range

For Lucheng District, station 1: Nanpu Station; station 2: Shizhan Station

spline model, which indicates that decreasing trends with increasing air pollutants were associated with reduced sperm progressive motility, total motility and semen volume in the entire group. The linear exposure–response curves between each air pollutant and sperm progressive motility, sperm total motility, and semen volume followed a monotonic trend ( $P_{\text{nonlinear}} > 0.05$ ), as shown by the linear trend results for quintiles of each pollutant exposure. Conversely, we found a strong inverse J-shaped nonlinear relationship between progressive sperm motility and exposure to SO<sub>2</sub> and CO. Additionally, a strong U-shaped nonlinear relationship was observed between sperm concentration and CO, although this relationship was not statistically significant ( $P_{\text{nonlinear}} > 0.05$ ).

We further assessed the associations of air pollutants with semen parameters during the 4 periods for the entire group (Fig. 3). We observed that air pollution during almost every period was associated with decreased sperm progressive motility, total motility and semen volume, and that the estimated negative impacts at lag 0–9 and 10–14 days were greater than those at lag 15–69 and

70–90 days (all  $P < 0.05$ ). Conversely, O<sub>3</sub> exposure at lag 0–9, 10–14 and 15–69 days was associated with increased sperm concentration (all  $P < 0.05$ ).

### Sensitivity analyses and stratified analyses

The results of the subgroup analysis are summarized in Table S3–S6 and Fig. S7–S10. The results of the interactions, exposure–response curves and associations with different periods in the subgroup were approximately the same as those of the entire group. The results of the analyses of the association between air pollutants and semen parameters stratified by age and season for the two groups during the 0–90 days before ejaculation are presented in Fig. S11. We found more significant negative associations between semen volume and air pollutants in men younger than 40 years of age. In addition, the positive associations of sperm concentration with air pollutants were more pronounced in spring and autumn.

**Table 3** Regression coefficients and 95% CIs of semen parameters associated with air pollutants exposure during 0–90 days before the date of semen examination for the study subjects

Semen quality parameter	Regression coefficients (95% CI)						
	Per IQR increase	Quintile of exposure					<i>P</i> <sub>trend</sub> <sup>a</sup>
		Q1	Q2	Q3	Q4	Q5	
<b>Progressive motility<sup>b</sup></b>							
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	– 22.351 (– 24.802, – 19.899)	0 (referent)	– 9.408 (– 13.953, – 4.863)	– 18.703 (– 23.500, – 13.906)	– 26.440 (– 31.357, – 21.524)	– 44.216 (– 49.802, – 38.630)	<0.001
PM <sub>10</sub> (µg/m <sup>3</sup> )	– 23.507 (– 26.364, – 20.650)	0 (referent)	– 13.192 (– 17.635, – 8.749)	– 21.088 (– 25.879, – 16.296)	– 25.848 (– 31.123, – 20.574)	– 46.948 (– 52.629, – 41.268)	<0.001
NO <sub>2</sub> (µg/m <sup>3</sup> )	– 14.663 (– 17.355, – 11.971)	0 (referent)	– 5.459 (– 10.000, – 0.919)	– 2.412 (– 7.321, 2.497)	– 14.273 (– 19.565, – 8.981)	– 25.722 (– 31.350, – 20.094)	<0.001
SO <sub>2</sub> (µg/m <sup>3</sup> )	– 17.926 (– 19.935, – 15.918)	0 (referent)	1.408 (2.984, 5.800)	– 2.077 (– 6.537, 2.383)	– 17.740 (– 22.095, – 13.386)	– 31.249 (– 35.842, – 26.657)	<0.001
O <sub>3</sub> (µg/m <sup>3</sup> )	– 14.866 (– 16.640, – 13.091)	0 (referent)	– 6.995 (– 11.888, – 2.102)	– 5.775 (– 10.740, – 0.811)	– 13.093 (– 18.233, – 7.953)	– 35.880 (– 41.255, – 30.506)	<0.001
CO (mg/m <sup>3</sup> )	– 21.859 (– 24.215, – 19.502)	0 (referent)	– 2.445 (– 6.678, 1.788)	2.241 (– 2.059, 6.540)	– 19.973 (– 24.401, – 15.546)	– 37.463 (– 41.948, – 32.978)	<0.001
<b>Total motility<sup>b</sup></b>							
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	– 44.904 (– 51.526, – 38.281)	0 (referent)	– 19.079 (– 31.340, – 6.818)	– 40.297 (– 53.238, – 27.356)	– 55.035 (– 68.298, – 41.772)	– 88.156 (– 103.225, – 73.086)	<0.001
PM <sub>10</sub> (µg/m <sup>3</sup> )	– 47.808 (– 55.5–03, – 40.113)	0 (referent)	– 30.385 (– 42.360, – 18.410)	– 46.797 (– 59.712, – 33.882)	– 55.769 (– 69.985, – 41.553)	– 96.479 (– 111.789, – 81.169)	<0.001
NO <sub>2</sub> (µg/m <sup>3</sup> )	– 29.096 (– 36.307, – 21.884)	0 (referent)	– 11.887 (– 24.051, 0.277)	– 2.925 (– 16.076, 10.226)	– 28.459 (– 42.636, – 14.282)	– 50.064 (– 65.142, – 34.986)	<0.001
O <sub>2</sub> (µg/m <sup>3</sup> )	– 36.346 (– 41.767, – 30.926)	0 (referent)	1.069 (– 10.790, 12.928)	– 3.721 (– 15.763, 8.321)	– 37.096 (– 48.853, – 25.338)	– 63.218 (– 75.617, – 50.818)	<0.001
O <sub>3</sub> (µg/m <sup>3</sup> )	– 30.293 (– 35.074, – 25.511)	0 (referent)	– 15.897 (– 29.070, – 2.725)	– 10.265 (– 23.631, 3.100)	– 26.251 (– 40.088, – 12.413)	– 73.584 (– 88.053, – 59.114)	<0.001
CO (mg/m <sup>3</sup> )	– 43.776 (– 50.145, – 37.408)	0 (referent)	– 8.083 (– 19.563, 3.398)	5.202 (– 6.459, 16.863)	– 41.208 (– 53.217, – 29.199)	– 76.830 (– 88.996, – 64.665)	<0.001
<b>Sperm concentration<sup>b</sup></b>							
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	0.167 (– 0.036, 0.370)	0 (referent)	0.125 (– 0.250, 0.501)	0.169 (– 0.228, 0.565)	0.283 (– 0.124, 0.689)	0.345 (– 0.117, 0.806)	0.123
PM <sub>10</sub> (µg/m <sup>3</sup> )	0.044 (– 0.192, 0.280)	0 (referent)	0.146 (– 0.221, 0.513)	0.267 (– 0.129, 0.662)	– 0.013 (– 0.449, 0.422)	0.303 (– 0.166, 0.772)	0.343
NO <sub>2</sub> (µg/m <sup>3</sup> )	0.028 (– 0.191, 0.247)	0 (referent)	– 0.107 (– 0.477, 0.262)	0.015 (– 0.385, 0.414)	– 0.094 (– 0.524, 0.337)	– 0.012 (– 0.470, 0.446)	0.997
SO <sub>2</sub> (µg/m <sup>3</sup> )	0.083 (– 0.083, 0.250)	0 (referent)	0.012 (– 0.352, 0.376)	– 0.126 (– 0.496, 0.244)	0.076 (– 0.285, 0.437)	0.178 (– 0.202, 0.559)	0.184
O <sub>3</sub> (µg/m <sup>3</sup> )	0.250 (0.104, 0.396)	0 (referent)	– 0.151 (– 0.554, 0.253)	0.041 (– 0.368, 0.450)	0.207 (– 0.217, 0.631)	0.229 (– 0.214, 0.672)	0.086
CO (mg/m <sup>3</sup> )	0.062 (– 0.133, 0.258)	0 (referent)	0.145 (– 0.210, 0.500)	– 0.333 (– 0.693, 0.028)	0.013 (– 0.358, 0.384)	0.185 (– 0.190, 0.561)	0.429

**Table 3** (continued)

Semen quality parameter	Regression coefficients (95% CI)							<i>P</i> <sub>trend</sub> <sup>a</sup>
	Per IQR increase	Quintile of exposure						
		Q1	Q2	Q3	Q4	Q5		
<b>Total sperm number<sup>b</sup></b>								
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	-0.242 (-0.518, 0.035)	0 (referent)	0.026 (-0.485, 0.537)	-0.281 (-0.821, 0.258)	-0.286 (-0.839, 0.267)	-0.458 (-1.087, 0.170)	0.088	
PM <sub>10</sub> (µg/m <sup>3</sup> )	-0.416 (-0.737, -0.096)	0 (referent)	-0.017 (-0.516, 0.482)	-0.194 (-0.732, 0.344)	-0.622 (-1.215, -0.030)	-0.467 (-1.105, 0.171)	0.071	
NO <sub>2</sub> (µg/m <sup>3</sup> )	-0.178 (-0.476, 0.120)	0 (referent)	-0.204 (-0.707, 0.299)	-0.317 (-0.860, 0.227)	-0.419 (-1.006, 0.167)	-0.455 (-1.079, 0.168)	0.151	
SO <sub>2</sub> (µg/m <sup>3</sup> )	-0.284 (-0.510, -0.057)	0 (referent)	0.064 (-0.431, 0.559)	-0.389 (-0.892, 0.114)	-0.371 (-0.862, 0.120)	-0.406 (-0.924, 0.112)	0.062	
O <sub>3</sub> (µg/m <sup>3</sup> )	-0.015 (-0.214, 0.185)	0 (referent)	-0.275 (-0.824, 0.274)	-0.101 (-0.657, 0.456)	-0.068 (-0.644, 0.509)	-0.493 (-1.096, 0.110)	0.127	
CO (mg/m <sup>3</sup> )	-0.400 (-0.666, -0.134)	0 (referent)	0.083 (-0.400, 0.565)	-0.450 (-0.940, 0.040)	-0.638 (-1.143, -0.134)	-0.479 (-0.990, 0.032)	0.008	
<b>Semen volume<sup>b</sup></b>								
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	-0.129 (-0.165, -0.092)	0 (referent)	-0.054 (-0.122, 0.014)	-0.160 (-0.231, -0.088)	-0.196 (-0.270, -0.123)	-0.255 (-0.339, -0.172)	<0.001	
PM <sub>10</sub> (µg/m <sup>3</sup> )	-0.134 (-0.177, -0.091)	0 (referent)	-0.081 (-0.147, -0.014)	-0.167 (-0.238, -0.096)	-0.180 (-0.259, -0.102)	-0.253 (-0.338, -0.168)	<0.001	
NO <sub>2</sub> (µg/m <sup>3</sup> )	-0.064 (-0.104, -0.025)	0 (referent)	-0.021 (-0.087, 0.046)	-0.106 (-0.178, -0.034)	-0.086 (-0.164, -0.008)	-0.142 (-0.225, -0.059)	0.001	
SO <sub>2</sub> (µg/m <sup>3</sup> )	-0.109 (-0.139, -0.079)	0 (referent)	-0.007 (-0.073, 0.058)	-0.066 (-0.133, 0.000)	-0.140 (-0.205, -0.075)	-0.183 (-0.252, -0.115)	<0.001	
O <sub>3</sub> (µg/m <sup>3</sup> )	-0.091 (-0.117, -0.064)	0 (referent)	-0.018 (-0.091, 0.055)	-0.038 (-0.112, 0.035)	-0.096 (-0.172, -0.019)	-0.213 (-0.292, -0.133)	<0.001	
CO (mg/m <sup>3</sup> )	-0.135 (-0.170, -0.100)	0 (referent)	-0.048 (-0.112, 0.016)	-0.013 (-0.078, 0.052)	-0.183 (-0.250, -0.117)	-0.210 (-0.278, -0.143)	<0.001	

CI: confidence interval; IQR: interquartile range

Q1: PM<sub>2.5</sub> (14.304–22.733), PM<sub>10</sub> (33.837–45.881), NO<sub>2</sub> (16.795–27.782), SO<sub>2</sub> (3.284–5.850), O<sub>3</sub> (30.235–53.617), CO (0.398–0.525)

Q2: PM<sub>2.5</sub> (22.734–27.762), PM<sub>10</sub> (45.882–53.534), NO<sub>2</sub> (27.783–33.029), SO<sub>2</sub> (5.851–7.031), O<sub>3</sub> (53.618–61.980), CO (0.526–0.618)

Q3: PM<sub>2.5</sub> (27.763–32.531), PM<sub>10</sub> (53.535–60.319), NO<sub>2</sub> (33.030–38.817), SO<sub>2</sub> (7.032–9.660), O<sub>3</sub> (61.981–67.521), CO (0.619–0.720)

Q4: PM<sub>2.5</sub> (32.532–41.021), PM<sub>10</sub> (60.320–72.259), NO<sub>2</sub> (38.818–45.491), SO<sub>2</sub> (9.661–12.789), O<sub>3</sub> (67.522–78.276), CO (0.721–0.841)

Q5: PM<sub>2.5</sub> (41.022–62.340), PM<sub>10</sub> (72.260–106.655), NO<sub>2</sub> (45.492–66.844), SO<sub>2</sub> (12.790–28.644), O<sub>3</sub> (78.277–119.639), CO (0.842–1.204)

The Regression and 95% CIs were estimated using multiple linear regression model, adjusting for age, ever having fathered a child, smoking, alcohol consumption, education, occupation, abstinence periods, season of sperm collection, average daily ambient temperature during 0–90 days and mean relative humidity during 0–90 days

<sup>a</sup>P-value for linear trend was tested based on variable containing the median value for each quintile

<sup>b</sup>Box-Cox transformation applied

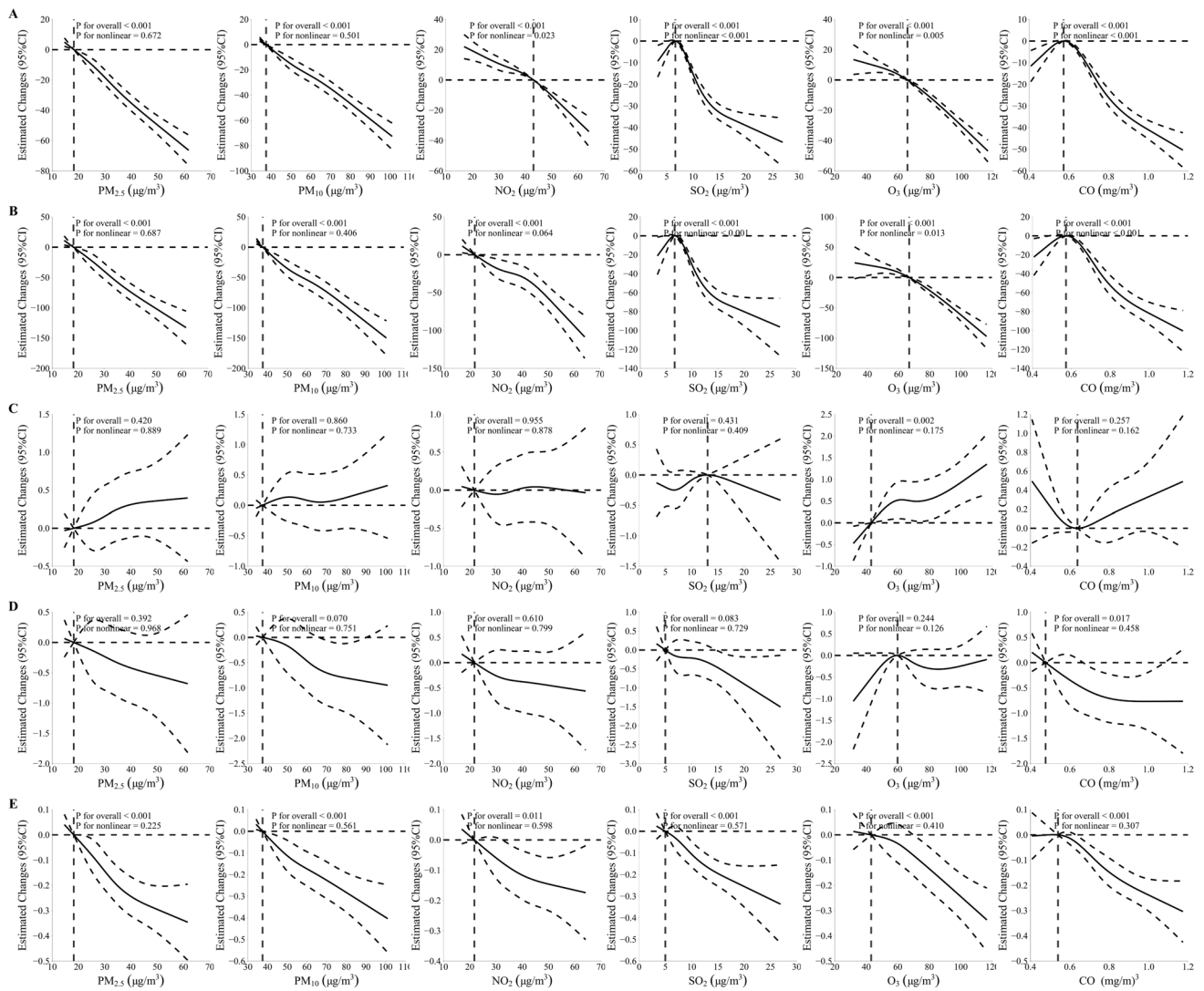
## Discussion

To our knowledge, the present study might be the first evaluation of the individual and joint associations of particulate and gaseous pollutants with semen parameters throughout and during all four periods of sperm development. After adjusting for important confounders, we found that air pollutant exposures had negative effects on sperm progressive motility, total motility, and sperm volume during every period. We also found a positive association of several air pollutants, particularly O<sub>3</sub>, with sperm concentration and

total sperm number. In addition, we investigated the joint effects of particulate matter and gaseous pollutants, but no statistically significant results were found. According to the stratified analyses by age and season, the negative effects of air pollutants on semen parameters were greater in males younger than 40 years of age, and the positive effects of air pollutants on sperm concentration were particularly pronounced in spring and autumn. These results were also validated in other subgroups.

We found that exposure to each air pollutant in the present study had negative effects on sperm progressive motility,



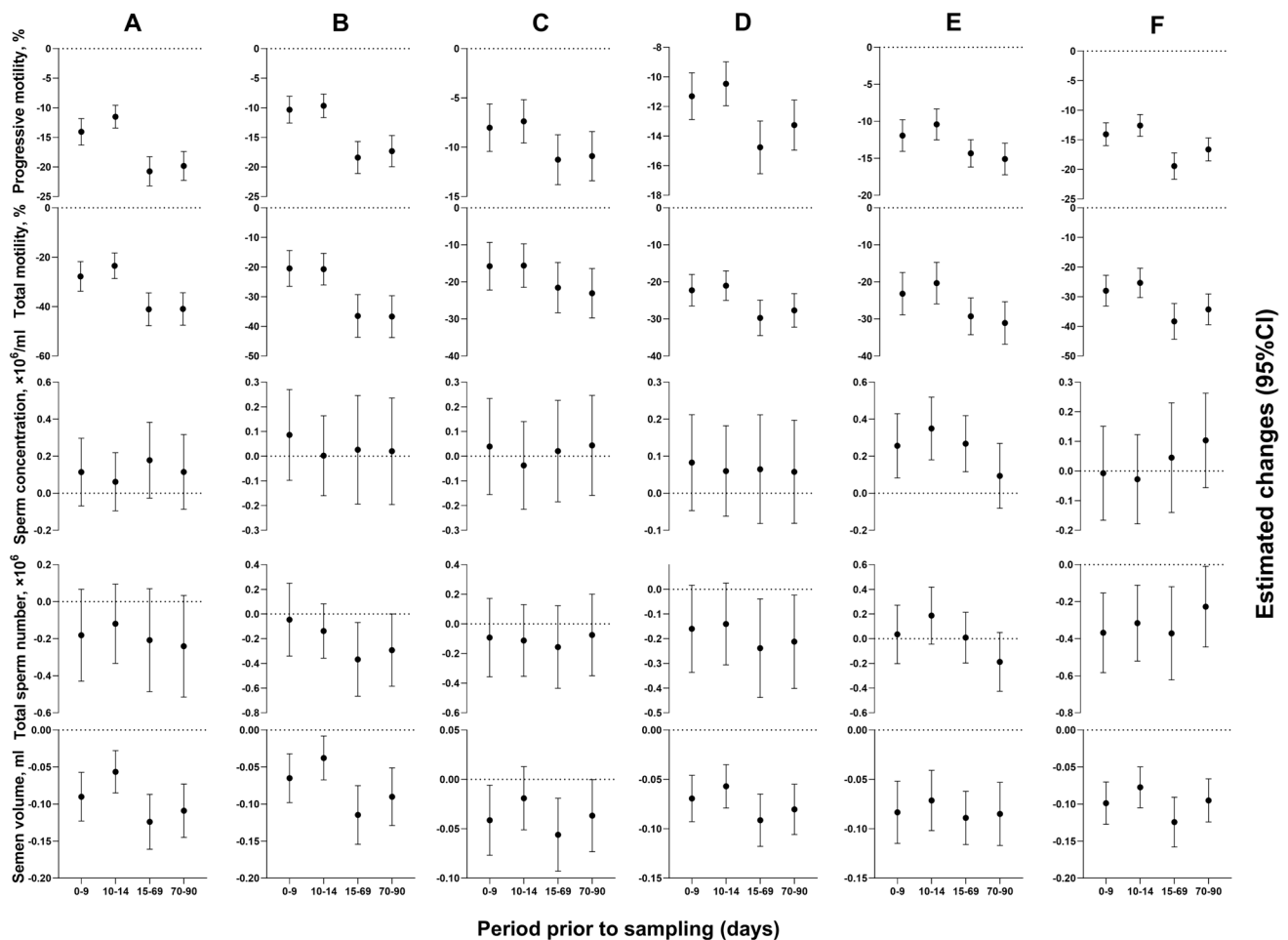


**Fig. 2** The exposure–response curves for the association between exposure to air pollutants (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub> and CO) and **A:** progressive motility (%), **B:** total motility (%), **C:** sperm concentration (10<sup>6</sup>/ml), **D:** total sperm number (10<sup>6</sup>), and **E:** semen volume(ml) during 0–90 days for the all participants. The data were fitted by multiple linear regression model using restricted cubic splines with 4 knots at the 5th, 35th, 65th, and 95th percentiles of

air pollutants, adjusted for age, ever having fathered a child, smoking, alcohol consumption, education, occupation, abstinence periods, season of sperm collection, average daily ambient temperature during 0–90 days and mean relative humidity during 0–90 days. All semen parameters were subjected Box–Cox transformation. The solid lines indicate  $\beta$ , the dashed lines indicate reference values and 95% CIs. P for nonlinear < 0.05 indicates a nonlinear relationship

total motility, and sperm volume during the entire development period, and the trends decreased, which is consistent with the findings of many existing studies (Dai et al. 2023; Huang et al. 2020; Sun et al. 2020; Wu et al. 2022; Zhang et al. 2023a). Currently, seven possible biological mechanisms are known to explain the reduction in semen quality caused by air pollutants, namely, reactive oxygen species (ROS) induction, apoptosis, inflammation, DNA methylation, blood–testis barrier disruption, hormonal disruption, and cellular hypoxia. For particulate matter (PM), many studies have demonstrated that exposure to PM can inhibit proliferation by inducing DNA damage through reactive oxygen

species and activating apoptotic signaling pathways (such as receptor-interacting protein kinase 1), resulting in the direct induction of death and mitochondrial structural disruption, leading to compromised energy metabolism and diminished sperm motility (Zhang et al. 2018; Liu et al. 2019). Inflammatory damage is also a possible cause of reduced semen quality in PM, which leads to a systemic inflammatory response by increasing a variety of proinflammatory factors (e.g., IL6 and TNF- $\alpha$ ), as well as damage to various tissues and organs (He et al. 2017). The accumulation of ROS due to the effects of PM causes an increase in 5-hydroxymethylcytosine (5-hmC) levels and regulates the onset of



**Fig. 3** Regression coefficients and 95% CIs of semen parameters associated with each IQR increase of lag 0–9, 10–14, 15–69 and 70–90 days exposure to air pollutants (A:  $PM_{2.5}$ , B:  $PM_{10}$ , C:  $NO_2$ , D:  $SO_2$ , E:  $O_3$  and F: CO) for the all the participants. Every exposure period was used in a separate multiple linear regression model

adjusted by age, ever having fathered a child, smoking, alcohol consumption, education, occupation, abstinence periods, season of sperm collection, average daily ambient temperature during different critical windows and mean relative humidity during different critical windows. All semen parameters were subjected Box–Cox transformation

demethylation (Sanchez-Guerra et al. 2015), which may affect the spermatogenesis process and semen quality (Uysal et al. 2016).  $PM_{2.5}$  can also affect sperm production and quality by altering the microenvironment of spermatogenesis by compromising the integrity of the blood–testosterone barrier (Wei et al. 2018). In addition, several animal studies have shown that polycyclic aromatic hydrocarbons absorbed in  $PM_{2.5}$  interfere with the hypothalamic–pituitary–gonadal axis, thereby affecting sperm development (Li et al. 2019). For gaseous pollutants, there is also a similar mechanism as for PM,  $NO_2$  and  $SO_2$  can independently cause oxidative damage to testicular tissue and impair the blood–testis barrier, resulting in impaired spermatogenesis and sperm DNA integrity (Meng and Bai 2004). Sokol et al. identified a number of potential mechanisms, such as oxidative stress caused by  $O_3$ , inflammatory responses, and the production of circulating toxic substances (Sokol et al. 2006). In addition, CO

can lead to cellular hypoxia, which can result in the down-regulation of estrogen receptor  $\alpha$  (ESR1) expression (Ziaei et al. 2005), interfering with normal estrogen signaling, and ultimately leading to reduced semen quality (Cooke et al. 2017), which is a unique biological mechanism of gaseous pollutants. We also observed a positive association between several air pollutants and sperm concentration and total sperm number, particularly  $O_3$ , which is consistent with the findings of several other studies (Zhou et al. 2014; Dai et al. 2023; Lao et al. 2018). A possible explanation for this result is the compensatory effect of air pollutants on semen quality. Specifically, low-level exposure increases the levels of follicle-stimulating hormone and luteinizing hormone (Lao et al. 2018; Tomei et al. 2009), which in turn supports spermatogenesis and increases the number and concentration of sperm.

Our study also revealed an inverse J-shaped association between sperm motility and exposure to SO<sub>2</sub> and CO, as well as a U-shaped relationship between sperm concentration and CO. The considerably wider 95% confidence interval suggested that the small sample sizes at lower exposure concentrations may be the cause of the increase in semen motility and the decrease in sperm concentration (Wu et al. 2017). However, caution should be exercised in interpreting and generalizing such nonlinear results due to the heterogeneity of pollutant exposures, populations, temperatures and monitoring instruments across regions (Qian et al. 2022).

In contrast to previous studies, we employed a regression model with multiplicative interaction terms to assess the joint associations of particulate and gaseous pollutants, which provides improved estimates (Liu et al. 2023). No joint associations were detected in our results, which is consistent with a previous study reporting an independent association (Zhang et al. 2023a). The possible reason for this is the unique biological mechanism by which CO affect semen quality through cellular hypoxia. Therefore, we speculate that this may be the predominant biological mechanism for the impact of CO on semen quality. This also leads to only individual associations of particulate and gaseous pollutants on semen quality. Similarly, we speculate that other gaseous pollutants may have biological mechanisms that differ from particulate matter in their effects on semen quality. However, further research is needed. Although particulate matter and gaseous pollutants did not interact on semen quality parameters, individual pollutants had a negative effect on semen quality. Given the above, there is still a need for better control of air pollution concentrations to enhance semen quality.

We observed that each air pollutants pollutant was negatively associated with sperm motility and semen volume, and some pollutants were positively associated with semen concentration or sperm number during the four periods, which is inconsistent with the findings of other studies (Table S7). This may be the outcome of a mixture of factors, including the population characteristics under study, the statistical analysis method employed, the study area, the concentration of the contaminant being examined, and the method used for assessing exposure. However, our findings showed that air pollutant exposure during four periods had a negative impact on sperm motility and semen volume, indicating the need to maintain control over pollutant concentrations at all times. Furthermore, the negative impacts at lag 0–9 and lag 10–14 days were greater than those at lag 15–69 and lag 70–90 days, respectively. Since the lag 10–14 days corresponds to the developmental stage of sperm motility, the negative impact on sperm motility was greater for both the lag 0–9 and lag 10–14 days.

According to the stratified analysis, we found more significant negative associations between semen volume and air pollutants in men younger than 40 years of age,

while the positive association between air pollutants and sperm concentration was more pronounced in spring and autumn. Seminal vesicles and fluid components originating from the prostate determine the volume of semen, which is strongly correlated with the functionality of the accessory glands (Mason et al. 2023). Significantly, age has an important influence on the functionality of accessory glands (Ajayi et al. 2023). In particular, when the age is older than 40 years, the semen volume is significantly lower than that in the other age groups (Wu et al. 2021). Therefore, when men are younger than 40 years of age, their accessory gland functionality is normal, and semen volume is more predominantly affected by air pollutants; when men are older than 40 years of age, the semen volume is more predominantly affected by the functionality of their accessory glands, and the effect of air pollutants may be relatively reduced or even absent. Furthermore, temperature is a significant factor that impacts the outcomes of our seasonal stratification analyses because previous studies have demonstrated that both high and low temperatures can adversely affect semen quality (Santi et al. 2018). High temperatures can impede the efficacy of both enzymatic and nonenzymatic antioxidants, trigger heatstroke in the testicles, and result in the excess generation of reactive oxygen species (Li et al. 2014), whereas heat shock proteins can be expressed in response to cold shock (Liu et al. 1994). These extreme temperatures can affect spermatogenesis and even lead to the death of spermatogonia (Perotti et al. 1990; Wang et al. 2007). As described, we recommend avoiding delayed childbearing and choosing to prepare for pregnancy in spring and autumn.

Compared to other studies, this is the first analysis of the potential interaction effect of particulate matter and gaseous pollutants on semen quality when they are jointly exposed. Although interactions were not detected, each pollutant exposure still had a negative effect on the semen quality parameters. Therefore, enhancing the control of each air pollutant is crucial to avoid damaging semen quality. In addition, we evaluated the association of pollutant exposure in periods other than the critical period with semen quality, effectively avoiding bias in assessing associations and incorrect periods. Moreover, we observed that pollutant exposure was associated with decreased semen quality in each period, which suggests that we should reduce exposure to pollutant concentrations regardless of the time period to improve semen quality in men, especially those who are planning to become pregnant. Finally, the results of our stratified analysis suggest avoiding delayed childbearing as well as choosing spring or autumn for pregnancy preparation, which is also very instructive for men planning a pregnancy.

Meanwhile, our study has several main limitations. First, the participants were from male infertility clinics, and were mainly infertile men; therefore, we need to cautiously promote the results to other populations and other regions.

Second, the use of site-monitored average daily exposure concentrations of pollutants to assess the exposure of study participants, may lead to inaccurate exposure assessments. Specifically, a patient's precise air pollutant exposure may be related to many social and lifestyle-related factors, such as indoor work exposure levels and occupational exposure levels (e.g., PAH and heavy metals). Therefore, in the future, more precise methods of assessing patient exposure to pollutants could be considered, such as the use of personal monitoring devices to monitor pollutant exposure. Despite exposure assessment errors, this remains an acceptable method in most cases due to the lack of more detailed information (Dai et al. 2023). Third, the impacts of the remaining confounding factors could not be ruled out due to a lack of data on confounding factors (e.g., body mass index (BMI) and occupational exposure concentrations).

## Conclusions

Our findings indicate that exposure to particulate and gaseous pollutants has no interaction on semen quality. In contrast, independent exposure to particulate matter and gaseous pollutants unfavorably impacts sperm motility and semen volume during various time periods (0–90, 0–9, 10–14, 15–69, and 70–90 days). Furthermore, our results suggest a probable positive association between pollutants and sperm concentration, particularly in spring and autumn. The results highlight the importance of reducing exposure to pollutant concentrations and selecting the most suitable season to improve semen quality in men of reproductive age.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s00420-024-02095-7>.

**Acknowledgements** We thank the China National Meteorological Data Service Center and the national real-time platform for city air quality monitoring of the China National Environmental Monitoring Centre for providing open monitoring data of meteorological factors and air quality.

**Funding** This work was supported by [Education Project of Zhejiang Province] and [Research Project of Wenzhou Medical University] (Grant numbers [Y202146906] and [KJHX2014]).

**Data Availability** The data that support the findings of this study are available from the Corresponding author, [Hong Huang], up on reasonable request.

## Declarations

**Conflicts of interest** The authors have no conflicts of interest to declare that are relevant to the content of this article.

**Ethics approval** Ethics approval for this study was obtained from the Ethics Committee of The First Affiliated Hospital at Wenzhou Medical University (issuing No. KY2023-R289).

**Consent to participate and publish** We obtained all the information recorded by trained physicians from the hospital information management system. All information was de-identified, and we do not need patients' informed consent.

## References

- Ajayi AF, Onaolapo MC, Omole AI, Adeyemi WJ, Oluwole DT (2023) Mechanism associated with changes in male reproductive functions during ageing process. *Exp Gerontol* 179:112232. <https://doi.org/10.1016/j.exger.2023.112232>
- Cooke PS, Nanjappa MK, Ko C, Prins GS, Hess RA (2017) Estrogens in male physiology. *Physiol Rev* 97(3):995–1043. <https://doi.org/10.1152/physrev.00018.2016>
- Dai X, Chen G, Zhang M, Mei K, Liu Y, Ding C et al (2023) Exposure to ambient particulate matter affects semen quality: a case study in Wenzhou. *China Androl* 11(3):444–455. <https://doi.org/10.1111/andr.13326>
- Gangwar RS, Bevan GH, Palanivel R, Das L, Rajagopalan S (2020) Oxidative stress pathways of air pollution mediated toxicity: recent insights. *Redox Biol* 34:101545. <https://doi.org/10.1016/j.redox.2020.101545>
- He M, Ichinose T, Yoshida S, Ito T, He C, Yoshida Y et al (2017) PM<sub>2.5</sub>-induced lung inflammation in mice: Differences of inflammatory response in macrophages and type II alveolar cells. *J Appl Toxicol*. <https://doi.org/10.1002/jat.3482>
- Huang G, Zhang Q, Wu H, Wang Q, Chen Y, Guo P et al (2020) Sperm quality and ambient air pollution exposure: a retrospective, cohort study in a Southern province of China. *Environ Res* 188:109756. <https://doi.org/10.1016/j.envres.2020.109756>
- Lao XQ, Zhang Z, Lau AKH, Chan TC, Chuang YC, Chan J et al (2018) Exposure to ambient fine particulate matter and semen quality in Taiwan. *Occup Environ Med* 75(2):148–154. <https://doi.org/10.1136/oemed-2017-104529>
- Li Y, Cao Y, Wang F, Li C (2014) Scrotal heat induced the Nrf2-driven antioxidant response during oxidative stress and apoptosis in the mouse testis. *Acta Histochem* 116(5):883–890. <https://doi.org/10.1016/j.acthis.2014.02.008>
- Li T, Wang Y, Hou J, Zheng D, Wang G, Hu C et al (2019) Associations between inhaled doses of PM<sub>2.5</sub>-bound polycyclic aromatic hydrocarbons and fractional exhaled nitric oxide. *Chemosphere*. <https://doi.org/10.1016/j.chemosphere.2018.11.196>
- Liu AY, Bian H, Huang LE, Lee YK (1994) Transient cold shock induces the heat shock response upon recovery at 37 degrees C in human cells. *J Biol Chem* 269(20):14768–14775. [https://doi.org/10.1016/S0021-9258\(17\)36691-7](https://doi.org/10.1016/S0021-9258(17)36691-7)
- Liu C, Chen R, Sera F, Vicedo-Cabrera AM, Guo Y, Tong S et al (2023) Interactive effects of ambient fine particulate matter and ozone on daily mortality in 372 cities: two stage time series analysis. *BMJ* 383:e075203. <https://doi.org/10.1136/bmj-2023-075203>
- Liu J, Liang S, Du Z, Zhang J, Sun B, Zhao T et al (2019) PM<sub>2.5</sub> aggravates the lipid accumulation, mitochondrial damage and apoptosis in macrophage foam cells. *Environ Pollut*. <https://doi.org/10.1016/j.envpol.2019.03.045>
- Lu ZH, Sun B, Wang YX, Wu YR, Chen YJ, Sun SZ et al (2023) Ozone exposure associates with sperm quality indicators: sperm telomere length as a potential mediating factor. *J Hazard Mater* 459:132292. <https://doi.org/10.1016/j.jhazmat.2023.132292>
- Ma Y, Zhang J, Cai G, Xia Q, Xu S, Hu C et al (2022) Inverse association between ambient particulate matter and semen quality in Central China: Evidence from a prospective cohort study of 15,112 participants. *Sci Total Environ* 833:155252. <https://doi.org/10.1016/j.scitotenv.2022.155252>



- Mason MM, Schuppe K, Weber A, Gurayah A, Muthigi A, Ramasamy R (2023) Ejaculation: the process and characteristics from start to finish. *Curr Sex Health Rep* 15(1):1–9. <https://doi.org/10.1007/s11930-022-00340-z>
- Meng Z, Bai W (2004) Oxidation damage of sulfur dioxide on testicles of mice. *Environ Res* 96(3):298–304. <https://doi.org/10.1016/j.envres.2004.04.008>
- Olesiejuk K, Chalubinski M (2023) How does particulate air pollution affect barrier functions and inflammatory activity of lung vascular endothelium? *Allergy* 78(3):629–638. <https://doi.org/10.1111/all.15630>
- Perotti M, Toddei F, Mirabelli F, Vairetti M, Bellomo G, McConkey DJ et al (1990) Calcium-dependent DNA fragmentation in human synovial cells exposed to cold shock. *FEBS Lett* 259(2):331–334. [https://doi.org/10.1016/0014-5793\(90\)80040-p](https://doi.org/10.1016/0014-5793(90)80040-p)
- Priti K, Shakya KS, Kumar P (2023) Selection of statistical technique for imputation of single site-univariate and multisite-multivariate methods for particulate pollutants time series data with long gaps and high missing percentage. *Environ Sci Pollut Res Int*. <https://doi.org/10.1007/s11356-023-27659-x>
- Qian H, Xu Q, Yan W, Fan Y, Li Z, Tao C et al (2022) Association between exposure to ambient air pollution and semen quality in adults: a meta-analysis. *Environ Sci Pollut Res Int* 29(7):10792–10801. <https://doi.org/10.1007/s11356-021-16484-9>
- Qiu Y, Yang T, Seyler BC, Wang X, Wang Y, Jiang M et al (2020) Ambient air pollution and male fecundity: a retrospective analysis of longitudinal data from a Chinese human sperm bank (2013–2018). *Environ Res* 186:109528. <https://doi.org/10.1016/j.envres.2020.109528>
- Sanchez-Guerra M, Zheng Y, Osorio-Yanez C, Zhong J, Chervona Y, Wang S et al (2015) Effects of particulate matter exposure on blood 5-hydroxymethylation: results from the Beijing truck driver air pollution study. *Epigenetics* 10(7):633–642. <https://doi.org/10.1080/15592294.2015.1050174>
- Santi D, Magnani E, Michelangeli M, Grassi R, Vecchi B, Pedroni G et al (2018) Seasonal variation of semen parameters correlates with environmental temperature and air pollution: a big data analysis over 6 years. *Environ Pollut* 235:806–813. <https://doi.org/10.1016/j.envpol.2018.01.021>
- Sicard P, Agathokleous E, Anenberg SC, De Marco A, Paoletti E, Calatayud V (2023) Trends in urban air pollution over the last two decades: a global perspective. *Sci Total Environ* 858(Pt 2):160064. <https://doi.org/10.1016/j.scitotenv.2022.160064>
- Sokol RZ, Kraft P, Fowler IM, Mamet R, Kim E, Berhane KT (2006) Exposure to environmental ozone alters semen quality. *Environ Health Perspect* 114(3):360–365. <https://doi.org/10.1289/ehp.8232>
- Sun S, Zhao J, Cao W, Lu W, Zheng T, Zeng Q (2020) Identifying critical exposure windows for ambient air pollution and semen quality in Chinese men. *Environ Res* 189:109894. <https://doi.org/10.1016/j.envres.2020.109894>
- Tomei G, Tomao E, Ciarrocca M, Rosati MV, Caciari T, Gamberale D et al (2009) Follicle-stimulating hormone levels in male workers exposed to urban chemical, physical, and psychosocial stressors. *Toxicol Ind Health* 25(6):395–402. <https://doi.org/10.1177/0748233709106466>
- Uysal F, Akkoyunlu G, Ozturk S (2016) DNA methyltransferases exhibit dynamic expression during spermatogenesis. *Reprod Biomed Online* 33(6):690–702. <https://doi.org/10.1016/j.rbmo.2016.08.022>
- Wang C, Cui YG, Wang XH, Jia Y, Sinha Hikim A, Lue YH et al (2007) Transient scrotal hyperthermia and levonorgestrel enhance testosterone-induced spermatogenesis suppression in men through increased germ cell apoptosis. *J Clin Endocrinol Metab* 92(8):3292–3304. <https://doi.org/10.1210/jc.2007-0367>
- Watanabe N, Oonuki Y (1999) Inhalation of diesel engine exhaust affects spermatogenesis in growing male rats. *Environ Health Perspect* 107(7):539–544. <https://doi.org/10.1289/ehp.99107539>
- Wei Y, Cao XN, Tang XL, Shen LJ, Lin T, He DW et al (2018) Urban fine particulate matter (PM<sub>2.5</sub>) exposure destroys blood-testis barrier (BTB) integrity through excessive ROS-mediated autophagy. *Toxicol Mech Methods*. <https://doi.org/10.1080/15376516.2017.1410743>
- WHO (2010) WHO laboratory manual for the examination and processing of human semen, 5th edn. World Health Organization, Geneva
- Wu L, Jin L, Shi T, Zhang B, Zhou Y, Zhou T et al (2017) Association between ambient particulate matter exposure and semen quality in Wuhan. *China Environ Int* 98:219–228. <https://doi.org/10.1016/j.envint.2016.11.013>
- Wu ZG, Chen WK, Fei QJ, Liu YL, Liu XD, Huang H et al (2021) Analysis of semen quality of 38 905 infertile male patients during 2008–2016 in Wenzhou. *China Asian J Androl* 23(3):314–318. [https://doi.org/10.4103/aja.aja\\_83\\_20](https://doi.org/10.4103/aja.aja_83_20)
- Wu W, Chen Y, Cheng Y, Tang Q, Pan F, Tang N et al (2022) Association between ambient particulate matter exposure and semen quality in fertile men. *Environ Health* 21(1):16. <https://doi.org/10.1186/s12940-022-00831-5>
- Xu R, Zhong Y, Li R, Li Y, Zhong Z, Liu T et al (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>
- Yang T, Deng L, Sun B, Zhang S, Xian Y, Xiao X et al (2021) Semen quality and windows of susceptibility: A case study during COVID-19 outbreak in China. *Environ Res* 197:111085. <https://doi.org/10.1016/j.envres.2021.111085>
- Zhang F, Li H, Xu W, Song G, Wang Z, Mao X et al (2023a) Sulfur dioxide may predominate in the adverse effects of ambient air pollutants on semen quality among the general population in Hefei. *China Sci Total Environ* 867:161472. <https://doi.org/10.1016/j.scitotenv.2023.161472>
- Zhang Y, Wei J, Liu C, Cao W, Zhang Z, Li Y et al (2023b) 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>
- Zhang J, Liu J, Ren L, Wei J, Duan J, Zhang L et al (2018) PM<sub>2.5</sub> induces male reproductive toxicity via mitochondrial dysfunction, DNA damage and RIPK1 mediated apoptotic signaling pathway. *Sci Total Environ*. <https://doi.org/10.1016/j.scitotenv.2018.03.383>
- Zhou N, Cui Z, Yang S, Han X, Chen G, Zhou Z et al (2014) Air pollution and decreased semen quality: a comparative study of Chongqing urban and rural areas. *Environ Pollut* 187:145–152. <https://doi.org/10.1016/j.envpol.2013.12.030>
- Ziaei S, Nouri K, Kazemnejad A (2005) Effects of carbon monoxide air pollution in pregnancy on neonatal nucleated red blood cells. *Paediatr Perinat Epidemiol* 19(1):27–30. <https://doi.org/10.1111/j.1365-3016.2004.00619.x>

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.