Associations Between Short-Term Ambient Particulate Matter Exposure and The Risk of Severe COVID-19

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Abstract

Background

Previous studies have suggested the relation between outdoor air pollution and the onset risk of Corona Virus Disease 2019 (COVID-19). However, there is a lack of data related to the severity of the disease, especially in China.

Methods

We recruited a group of COVID-19 patients diagnosed in a recent large-scale outbreak caused by Delta variants in eastern China. We collected ambient air pollution data of the same period where the case occurred and applied a generalized linear model (GLM) to analyze the effects of short-term outdoor ambient particulate matter (PM) exposure on the risk of severe COVID-19.

Results

A total of 476 confirmed adult patients were recruited, of which 42 (8.82%) had a severe illness. With a unit increase in PM_{10} , the risk of severe COVID-19 increased by 47.64% (95% confidence interval [CI]: 27.67, 70.73) at lag 0-14 days, 65.00% (95% CI: 35.18, 101.40) at lag 0-21 days, and 69.44% (95% CI: 37.03, 109.50) at lag 0-28 days, respectively. The association remained significant at lag 0-14 days or 0-28 days in the multi-pollutant models. With a unit increase in $PM_{2.5}$, the risk of severe COVID-19 increased by 49.47% (95% CI: 19.61, 86.78) at lag 0-14 days, 97.61% (95% CI: 45.92, 167.60) at lag 0-21 days, and 120.27% (95% CI: 56.53, 209.98) at lag 0-28 days, respectively. The association remained significant at lag 0-21 days or 0-28 days in the multi-pollutant models.

Conclusions

Our results indicated that short-term exposure to outdoor PM was positively related to the risk of severe COVID-19, and reducing air pollution may contribute to the control of COVID-19.

Background

In December 2019, the Corona Virus Disease 2019 (COVID-19), caused by the SARS-CoV-2, was first reported in Wuhan and escalated into a global pandemic [1, 2]. There is no doubt that COVID-19 has posed a severe threat to global health. Patients with COVID-19 can be categorized into mild, moderate, severe, and critical based on condition. The prognosis of severe and critical patients is poor [3], and the risk factors include older age and hypertension [4].

The particulate matter (PM), produced by the combustion of biomass and diesel, and spark-ignited vehicle emissions, is tightly correlated with environmental pollution [5]. In particular, PM with an aerodynamic diameter $\leq 10 \mu\text{m}$ (PM_{10}) or $\leq 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$) have attracted widespread public attention as they are inhalable [6, 7]. PM was positively associated with the risk of communicable and non-communicable diseases [8–10]. A global time-series study showed that short-term PM exposure contributed to an increased cardiovascular and respiratory mortality [11]. Recently, several studies have revealed the possible links between PM exposure and the onset risk of COVID-19 [12, 13]. For example, a multi-city study in China found that for each $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$, the risk of COVID-19 increased by 5% and 6%, respectively [14]. Another study in Germany showed that every $1 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ was associated with 52.38 and 199.46 more confirmed COVID-19 cases per 100,000 inhabitants, respectively [15]. The associations between ambient PM exposure and the onset risk of COVID-19 have been ardently discussed. Nevertheless, studies on the effects of outdoor PM exposure on the severity of COVID-19 are insufficient, notably in China.

On July 20, 2021, Nanjing Lukou International Airport identified nine domestic COVID-19 cases through regular screening. Subsequently, the disease spread rapidly to surrounding cities, resulting in hundreds of confirmed cases in four cities in Jiangsu Province, including Nanjing, Yangzhou, Huaian, and Suqian. The scale of this epidemic in China is second only to the Wuhan epidemic in 2020. The genome sequencing confirmed that the pathogen causing this epidemic was the SARS-CoV-2 B.1.617.2 (Delta) variant, which initially appeared in India [16]. Thus, we collected data of COVID-19 patients identified in this outbreak and ambient air pollution data of the same period where the case occurred, aiming to evaluate the relationships between short-term ambient PM exposure and the risk of COVID-19 severity.

Methods

Study population

We collected data of COVID-19 patients admitted to Nanjing Public Health Medical Center from July 20, 2021, to August 17, 2021. All of them came from Nanjing, Yangzhou, Huaian, or Suqian, and were related to the recent outbreak of COVID-19 that originated in Nanjing Lukou international airport. The location of the four cities is shown in Figure 1. The inclusive criteria were as follows: (1) patients aged ≥ 18 years; (2) they were infected with the Delta variant. We collected general characteristics of patients including city, sex, age, current or past hypertension (yes or no), current or past diabetes (yes or no), current or past heart disease (yes or no), current or past carcinoma (yes or no), current or past COPD (yes or no), current or past asthma (yes or no), current or past autoimmune disease (yes or no), vaccination status (unvaccinated, partially vaccinated, or fully vaccinated), and days between onset and hospitalization. Patients were defined as fully vaccinated if they had received two doses of vaccination with the interval between the two doses ≥ 21 days and the onset date was ≥ 14 days from the second dose [17].

The diagnosis and classification of COVID-19 referred to the "Guidelines for Diagnosis and Treatment of COVID-19 (Trial Eighth Edition)" issued by the National Health Commission (<http://www.nhc.gov.cn/>). Patients were categorized as mild, moderate, severe, and critical based on the condition. In the current study, we combined severe and critical together and named them as severe.

Air pollution data

We extracted daily concentration data of six ambient air pollutants, including PM₁₀, PM_{2.5}, SO₂, NO₂, CO, and O₃ (the concentration of O₃ was the maximum 8-hour moving average) in four cities between June 15, 2021, and August 15, 2021, from National urban air quality real-time release platform (<http://106.37.208.233:20035/>). Except that the unit of CO concentration was mg/m³, the concentration of other pollutants was µg/m³.

Statistical analysis

We applied the generalized linear model (GLM) with the logit connect function to estimate the effects of short-term PM exposure on the severity of COVID-19. The GLM has been widely used in exploring the associations between air pollutants and health outcomes [18, 19]. Covariates adjusted in the model included city, sex, age, current or past hypertension, current or past diabetes, current or past heart disease, current or past carcinoma, current or past COPD, current or past asthma, current or past autoimmune disease, vaccination status, and days between onset and hospitalization. Previous studies showed that PM exposure might have lag effects on health [20, 21]. Thus, we calculated the moving average concentration of PM to describe personal PM exposure level according to the onset date of COVID-19 and place of residence [20, 22]. For instance, if the onset date was August 1, we extracted the daily average concentration of PM in the same place from July 4 to August 1. Then, we calculated the average concentration from July 25 to August 1 as the 8-day moving average, from July 18 to August 1 as the 15-day moving average, and from July 4 to August 1 as the 29-day moving average. We used four different lag times, including lag 0-7 days (8-day moving average), lag 0-14 days (15-day moving average), lag 0-21 days (22-day moving average), and lag 0-28 days (29-day moving average) [22, 23]. The strength of association was expressed as the changes in the risk of severe COVID-19 and their 95% confidence intervals (CIs) for a unit increase in PM concentration.

We conducted two sensitivity analyses to examine the robustness of the relationships between PM exposure and severe COVID-19. First, as mentioned above, we estimated the association at different lag times. Second, we adjusted other air pollutants to construct multi-pollutant models. We used the Spearman rank correlation test to evaluate the correlation between air pollutants. Only pollutants with $|r| < 0.7$ could enter into the multi-pollutant models to address the multiple collinearity problem [24]. Moreover, in order to ensure the comparability of the models, only pollutants with all $|r| < 0.7$ at four lag times were entered into the multi-pollutant models. For example, if the $|r|$ between SO₂ and PM₁₀ were all < 0.7 at four lag times, while the $|r|$ between NO₂ and PM₁₀ were < 0.7 at only three lag times, SO₂ could enter into the multi-pollutant models while NO₂ could not.

Additionally, we performed a subgroup analysis to explore whether the effects of PM exposure on the risk of severe COVID-19 were modified by sex or age. The difference in effects between subgroups was

$$|\beta_1 - \beta_2| / \sqrt{SE_1^2 + SE_2^2},$$

examined by the following formula: where β_1 and β_2 were the estimated effects, and SE_1 and SE_2 were their standard errors. The difference was considered to be statistically significant if the value was >1.96 [25]. All analyses were performed using R software version 4.0.4 (<https://www.r-project.org/>). The significance level was 0.05.

Results

Characteristics of the patients

A total of 533 COVID-19 patients were admitted, and 476 patients that met the inclusion criteria were included in the current study, of which 273 (57.35%) came from Yangzhou, 189 (39.71%) came from Nanjing, 12 (2.52%) came from Huaian, and 2 (0.42%) came from Suqian (Figure 1). Among them, 42 (8.82%) were classified as severe, 289 (60.71%) were females, 298 (62.61%) were 18-59 years old, 109 (22.90%) had hypertension, 43 (9.03%) had diabetes, 21 (4.41%) had heart disease, 11 (2.31%) had carcinoma, 3 (0.63%) had COPD, 9 (1.89%) had asthma, 5 (1.05%) had autoimmune disease, and 151 (31.72%) patients were fully vaccinated.

Concentration of PM₁₀ and PM_{2.5} in four cities

Between June 15, 2021, and August 15, 2021, the median (interquartile range) concentration of PM₁₀ was 34.00 (20.25) µg/m³ in Yangzhou, 31.50 (17.25) µg/m³ in Nanjing, 28.00 (19.75) µg/m³ in Huaian, and 34.00 (20.50) µg/m³ in Suqian (Table 2). The median (interquartile range) concentration of PM_{2.5} was 17.50 (13.25) µg/m³ in Yangzhou, 15.50 (12.00) µg/m³ in Nanjing, 16.00 (11.25) µg/m³ in Huaian, and 17.50 (12.25) µg/m³ in Suqian (Table 2).

Table 1
Characteristics of 476 COVID-19 patients with or without severe illness.

Characteristics	Non-severe illness	Severe illness	<i>p</i> ^a
	n (%) or median (interquartile range)	n (%) or median (interquartile range)	
Gender			0.247
Male	167 (89.30)	20 (10.70)	
Female	267 (92.39)	22 (7.61)	
Age group (years)			<0.001
18-59	286 (95.97)	12 (4.03)	
≥60	148 (83.15)	30 (16.85)	
Medical conditions			
Hypertension	94 (86.24)	15 (13.76)	0.038
Diabetes	35 (81.40)	8 (18.60)	0.037
Heart disease	16 (76.19)	5 (23.81)	0.037
Carcinoma	9 (81.82)	2 (18.18)	0.252
COPD	1 (33.33)	2 (66.67)	0.022
Asthma	8 (88.89)	1 (11.11)	0.568
Autoimmune disease	4 (80.00)	1 (20.00)	0.371
Vaccination status			<0.001
Unvaccinated	114 (84.44)	21 (15.56)	
Partially vaccinated	170 (89.47)	20 (10.53)	
Fully vaccinated	150 (99.34)	1 (0.66)	
Days between onset and hospitalization	3.00 (4.00)	3.00 (3.00)	0.152
^a : As appropriate, a comparison between groups was made using Chi-square test, Fisher's exact test or Mann-Whitney U test.			

Table 2
Daily average concentration of air pollutants in four cities in Jiangsu between June 15, 2021 and August 15, 2021.

City	Air pollutant	Minimum	Q ₂₅	Median	Mean	Q ₇₅	Maximum
Yangzhou	PM ₁₀ (μg/m ³)	8.00	27.50	34.00	37.35	47.75	82.00
	PM _{2.5} (μg/m ³)	5.00	13.00	17.50	19.39	26.25	38.00
	SO ₂ (μg/m ³)	7.00	9.00	9.00	9.89	11.00	14.00
	NO ₂ (μg/m ³)	4.00	10.00	18.00	18.03	24.25	38.00
	CO (mg/m ³)	0.30	0.40	0.50	0.51	0.60	0.90
	O ₃ (μg/m ³)	51.00	81.75	107.00	120.55	161.25	268.00
Nanjing	PM ₁₀ (μg/m ³)	6.00	24.75	31.50	33.63	42.00	71.00
	PM _{2.5} (μg/m ³)	3.00	11.00	15.50	17.68	23.00	47.00
	SO ₂ (μg/m ³)	3.00	5.00	5.00	5.16	6.00	7.00
	NO ₂ (μg/m ³)	6.00	14.75	18.50	18.92	24.25	32.00
	CO (mg/m ³)	0.30	0.48	0.50	0.56	0.70	0.90
	O ₃ (μg/m ³)	48.00	84.25	105.50	116.77	146.75	207.00
Huaian	PM ₁₀ (μg/m ³)	8.00	20.75	28.00	30.44	40.50	68.00
	PM _{2.5} (μg/m ³)	6.00	12.00	16.00	18.34	23.25	40.00
	SO ₂ (μg/m ³)	3.00	4.00	4.00	4.37	5.00	8.00
	NO ₂ (μg/m ³)	4.00	8.00	10.00	12.00	13.25	35.00
	CO (mg/m ³)	0.20	0.20	0.40	0.36	0.43	1.00
	O ₃ (μg/m ³)	42.00	72.75	103.50	108.76	133.00	231.00
Suqian	PM ₁₀ (μg/m ³)	9.00	26.00	34.00	36.63	46.50	78.00
	PM _{2.5} (μg/m ³)	5.00	13.00	17.50	18.65	25.25	40.00

City	Air pollutant	Minimum	Q ₂₅	Median	Mean	Q ₇₅	Maximum
	SO ₂ (µg/m ³)	2.00	4.00	5.00	5.16	6.00	9.00
	NO ₂ (µg/m ³)	2.00	6.00	9.00	10.26	13.25	25.00
	CO (mg/m ³)	0.30	0.40	0.40	0.47	0.60	0.90
	O ₃ (µg/m ³)	44.00	84.75	108.50	116.85	145.25	259.00

PM₁₀ and severe COVID-19

In the single-pollutant models, PM₁₀ was positively related to the risk of severe COVID-19 at lag 0-14 days, lag 0-21 days, and lag 0-28 days. The maximum effect was at lag 0-28 days. For a unit increase in PM₁₀, the risk of severe COVID-19 increased by 69.44% (95% CI: 37.03, 109.50) (Table 3).

Table 3

Changes in the risk of severe COVID-19 and their 95% CIs for a unit increase in the concentration of particulate matter.

Lag time	PM ₁₀		PM _{2.5}	
	Single-pollutant model ^a	Multi-pollutant model ^b	Single-pollutant model ^a	Multi-pollutant model ^b
Lag 0-7 days	3.64 (-4.29, 12.22)	7.44 (-6.25, 23.13)	-7.69 (-18.91, 5.08)	-12.61 (-24.03, 0.53)
Lag 0-14 days	47.64 (27.67, 70.73)	43.02 (5.26, 94.32)	49.47 (19.61, 86.78)	15.33 (-12.14, 51.38)
Lag 0-21 days	65.00 (35.18, 101.40)	10.02 (-33.65, 82.42)	97.61 (45.92, 167.60)	69.08 (22.12, 134.10)
Lag 0-28 days	69.44 (37.03, 109.50)	124.99 (14.22, 343.21)	120.27 (56.53, 209.98)	104.79 (28.57, 226.19)
^a : Adjusted for city, sex, age, current or past hypertension, current or past diabetes, current or past heart disease, current or past carcinoma, current or past COPD, current or past asthma, current or past autoimmune disease, vaccination status, and days between onset and hospitalization.				
^b : Based on single-pollutant models, additionally adjusted for other air pollutants at the same lag time.				

In the multi-pollutant models, PM₁₀ was positively correlated with the risk of severe COVID-19 at lag 0-14 days and lag 0-28 days. The maximum effect was also at lag 0-28 days. For a unit increase in PM₁₀, the risk of severe COVID-19 increased by 124.99% (95% CI: 14.22, 343.21) (Table 3).

PM_{2.5} and severe COVID-19

In the single-pollutant models, PM_{2.5} was positively related to the risk of severe COVID-19 at lag 0-14 days, lag 0-21 days, and lag 0-28 days. The maximum effect was at lag 0-28 days. For a unit increase in PM_{2.5}, the risk of severe COVID-19 increased by 120.27% (95% CI: 56.53, 209.98) (Table 3).

In the multi-pollutant models, PM_{2.5} was positively correlated with the risk of severe COVID-19 at lag 0-21 days and lag 0-28 days. The maximum effect was also at lag 0-28 days. For a unit increase in PM_{2.5}, the risk of severe COVID-19 increased by 104.79% (95% CI: 28.57, 226.19) (Table 3).

Subgroup analysis

The associations between PM₁₀ and the risk of severe COVID-19 remained significant in different gender or age groups at lag 0-14 days, lag 0-21 days, and lag 0-28 days. The maximum effect was observed at lag 0-28 days. For a unit increase in PM₁₀, the risk of severe COVID-19 increased by 132.03% (95% CI: 43.18, 276.01) in males, 55.85% (95% CI: 18.89, 104.29) in females, 94.80% (95% CI: 22.35, 210.16) in patients aged 18-59 years, and 64.21% (95% CI: 26.01, 114.00) in patients aged over 60 years. The effects of PM₁₀ on the risk of severe COVID-19 were not significantly modified by sex or age ($P>0.05$) (Table 4).

Table 4

Changes in the risk of severe COVID-19 and their 95% CIs for a unit increase in PM₁₀ concentration in subgroups, based on the single-pollutant models.

Lag time	Male	Female	18-59 years old	≥60 years old
Lag 0-7 days	3.51 (-8.59, 17.21)	5.11 (-5.99, 17.52) ^a	11.16 (-7.26, 33.23)	0.84 (-8.36, 10.96) ^a
Lag 0-14 days	86.82 (32.53, 163.37)	38.53 (15.22, 66.55) ^a	52.12 (14.62, 101.88)	47.30 (21.83, 78.10) ^a
Lag 0-21 days	112.04 (36.75, 228.79)	50.08 (17.63, 91.48) ^a	89.84 (17.49, 206.73)	57.48 (24.98, 98.41) ^a
Lag 0-28 days	132.03 (43.18, 276.01)	55.85 (18.89, 104.29) ^a	94.80 (22.35, 210.16)	64.21 (26.01, 114.00) ^a
^a : There was no significant difference in the effects between the subgroups ($P>0.05$).				

The associations between PM_{2.5} and the risk of severe COVID-19 remained significant in different gender or age groups at lag 0-14 days, lag 0-21 days, and lag 0-28 days. The maximum effect was observed at lag 0-28 days. For a unit increase in PM_{2.5}, the risk of severe COVID-19 increased by 200.72% (95% CI: 58.61, 470.16) in males, 109.13% (95% CI: 29.13, 238.71) in females, 153.30% (95% CI: 25.43, 411.54) in patients aged 18-59 years, and 122.09% (95% CI: 40.50, 251.05) in patients aged over 60 years. The effects of PM_{2.5} on the risk of severe COVID-19 were not significantly modified by sex or age ($P>0.05$) (Table 5).

Table 5

Changes in the risk of severe COVID-19 and their 95% CIs for a unit increase in PM_{2.5} concentration in subgroups, based on the single-pollutant models.

Lag time	Male	Female	18-59 years old	≥60 years old
Lag 0-7 days	-8.45 (-25.26, 12.14)	-5.55 (-21.41, 13.50) ^a	4.42 (-19.88, 36.11)	-12.42 (-25.52, 2.98) ^a
Lag 0-14 days	65.83 (15.08, 138.96)	51.21 (8.91, 109.93) ^a	48.62 (5.38, 109.59)	51.00 (6.63, 113.83) ^a
Lag 0-21 days	156.15 (46.81, 346.93)	89.46 (23.92, 189.66) ^a	125.06 (22.24, 314.35)	92.50 (29.23, 186.73) ^a
Lag 0-28 days	200.72 (58.61, 470.16)	109.13 (29.13, 238.71) ^a	153.30 (25.43, 411.54)	122.09 (40.50, 251.05) ^a
^a : There was no significant difference in the effects between the subgroups ($P > 0.05$).				

Discussion

In this study, we conducted a time-series study among 476 COVID-19 patients caused by the Delta SARS-CoV2 variant to explore the effects of short-term PM exposure on the risk of severe COVID-19. We observed that short-term exposure to PM was positively associated with the risk of severe COVID-19, and either sex or age did not alter the association. To our knowledge, this is the first individual-level study to evaluate the relationship between short-term PM exposure and the risk of severe COVID-19 in China.

A multicenter study in 33 European countries found that PM_{2.5} was positively related to the number of COVID-19 deaths [26]. Although this study was qualitative and did not consider potential confounding factors, it provided evidence of PM exposure contributing to a poor prognosis of COVID-19. A global research based on satellite data showed that approximately 15% of the global COVID-19 mortality (27% in East Asia, 19% in Europe, and 17% in North America) were attributed to the long-term PM_{2.5} exposure [27]. A study in California reported that a wildfire increased the PM_{2.5} concentration in ten counties by 220.71%, and subsequently, the number of deaths from COVID-19 in these areas increased by 148.2% [28]. Another study in London showed that environmental PM_{2.5} was positively correlated with the mortality of COVID-19. For a unit increase in PM_{2.5}, the number of deaths due to COVID-19 increased by 2.3% [29]. Another study explored the relationships between long-term exposure to PM_{2.5} and the hospitalization of COVID-19 in Cincinnati and found that a unit increase in 10-year average PM_{2.5} concentration was correlated with an 18% higher hospitalization rate [30]. Although most of the previous studies were ecological and focused on the COVID-19 mortality or hospitalization rate, their findings indirectly supported that PM exposure was related to the severity of COVID-19. Moreover, our results showed that the effect of PM_{2.5} seemed to be stronger than PM₁₀. This may be attributed to the smaller

particle size of PM_{2.5}, which can penetrate deep into the alveoli and bronchioles, and thus has more potent biological toxicity [11].

The following reasons may explain the potential links between PM and severe COVID-19. Firstly, PM suspended in the air, especially for PM_{2.5}, may not only carry the SARS-CoV-2, but also enhance the attachment and replication of the virus in the bronchus by damaging the integrity of bronchial epithelial cells [30]. Secondly, as pointed by Domingo et al., SARS-CoV-2 attached to PM may survive longer and be more aggressive in the immune system, which was aggravated by exposure to high concentrations of air pollutants [31]. Thirdly, as mentioned before, PM_{2.5} can reach the alveoli, thereby delivering the SARS-CoV-2 to the target type II alveolar cells [30]. Previous studies have shown that PM, especially PM_{2.5}, can stimulate activated alveolar macrophages and then induce pro-inflammatory cytokines production and release, thus aggravating the allergic inflammation in the lungs [32]. Fourthly, the metals and polycyclic aromatic hydrocarbons that make up PM_{2.5} facilitate the production of free radicals, which may oxidize alveolar cells. Excessive free radicals would weaken cellular antioxidant capacity, leading to lipid peroxidation and increased intracellular calcium concentration, further inducing cellular damage [33]. Finally, the SARS-CoV-2 entered the cell through binding to the angiotensin-converting enzyme 2 (ACE2) receptor, and this process can be enhanced by PM exposure [13]. The binding of the SARS-CoV-2 and the ACE2 receptor resulted in the down-regulation of the latter. The ACE2 mediated the transformation of angiotensin II to angiotensin 1-7 through the G protein-coupled receptor pathway and worked with angiotensin 1-7 by anti-inflammatory and antioxidant to protect the body. The down-regulation of ACE2 decreased its protective effect and worsened the effect of angiotensin II [34].

Our study had several limitations. First, we estimated the PM exposure level of each patient based on the monitoring data from the fixed sites, which may not accurately reflect the individual exposure. Second, other factors related to the severity of COVID-19, which were not considered in the analysis, may affect the results. Third, since the epidemic was under control for a short time, the sample size of this study was relatively small, especially for the number of severe patients. The association between PM and severe COVID-19 needs to be further confirmed in future studies.

Conclusions

Our results showed that short-term PM exposure was positively correlated with the risk of severe COVID-19, and such an association was not significantly altered by sex or age. Curbing outdoor PM pollution will help decrease the burden of COVID-19 and benefit the prognosis.

Abbreviations

COVID-19

Corona Virus Disease 2019

GLM

generalized linear model

PM
particulate matter
CI
confidence interval
ACE2
angiotensin-converting enzyme 2.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

ZL, BT, and JW conceived, initiated, and led the study. ZL, BT, MZ, ZH, and YY collected the data. ZL, BT, and JW analyzed the data with input from all the authors. ZL and JW prepared the manuscript. All authors reviewed and approved the manuscript.

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Availability of data and materials

Please contact the author for the original data.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Nanjing Public Health Medical Center.

Consent for publication

Not applicable.

Competing interests

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

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Figures

Figure 1

The geographic location of the four cities in Jiangsu Province.