

Living near a Major Road in Beijing: Association with Lower Lung Function, Airway Acidification, and Chronic Cough

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Abstract

Background: The effects of near-road pollution on lung function in China have not been well studied. We aimed to investigate the effects of long-term exposure to traffic-related air pollution on lung function, airway inflammation, and respiratory symptoms.

Methods: We enrolled 1003 residents aged 57.96 ± 8.99 years living in the Shichahai Community in Beijing. Distances between home addresses and the nearest major roads were measured to calculate home-road distance. We used the distance categories 1, 2, and 3, representing <100 m, 100–200 m, and >200 m, respectively, as the dose indicator for traffic-related air pollution exposure. Lung function, exhaled breath condensate (EBC) pH, and interleukin 6 levels were measured. As a follow-up, 398 participants had a second lung function assessment about 3 years later, and lung function decline was also examined as an outcome. We used regression analysis to assess the impacts of home-road distance on lung function and respiratory symptoms. As the EBC biomarker data were not normally distributed, we performed correlation analysis between home-road distance categories and EBC biomarkers.

Results: Participants living a shorter distance from major roads had lower percentage of predicted value of forced expiratory volume in 1 s (FEV1% -1.54 , 95% confidence interval [CI]: -0.20 to -2.89). The odds ratio for chronic cough was 2.54 (95% CI: 1.57–4.10) for category 1 and 1.97 (95% CI: 1.16–3.37) for category 2, compared with category 3. EBC pH was positively correlated with road distance (rank correlation coefficient of Spearman [r_s] = 0.176, $P < 0.001$).

Conclusions: Long-term exposure to traffic-related air pollution in people who live near major roads in Beijing is associated with lower lung function, airway acidification, and a higher prevalence of chronic cough. EBC pH is a potential useful biomarker for evaluating air pollution exposure.

Key words: Air Pollution; Airway Inflammation; Chronic Cough; Exhaled Breath Condensate; Lung Function

INTRODUCTION

Air pollution in megacities is closely related to traffic emissions. Environmental studies have found that the concentration of traffic-related air pollutants decreases with increased distance from the road.^[1] Home-road distance has been used as an index of air pollution exposure in various studies. Several large cohort studies^[2-5] have indicated that living near a major road is associated with lower lung function. A recent study by Rice *et al.*^[4] found an accelerated forced expiratory volume in 1 s (FEV1) decline in participants living closer to a major road.

However, these studies were conducted in Europe and the US, where air pollution is relatively mild. China is experiencing rapid development, which along with economic

boom brings serious air pollution. Currently, there is no information about the relationship between home-road distance and lung function in the Chinese population.

Besides lung function, epidemiological studies^[5,6] have also found a linkage between home-road distance and respiratory symptoms or diseases. It has been inferred that airway

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inflammation might play a crucial role in the pathogenesis of airway diseases.^[7] Thus, we hypothesized that airway inflammation biomarkers might be associated with both lung function and home-road distance.

Beijing, famous for its smog in recent years, serves as an ideal place to study traffic-related air pollution and lung function decline, and their relationship with inflammatory biomarkers.

METHODS

Study population

The study cohort was sourced from a previous epidemiological study of chronic obstructive pulmonary disease (COPD) we performed in 2009. At that time, long-term (≥ 3 years) residents in the Shichahai Community in Beijing over 35 years of age were invited to take part in the study. Participants were selected using a stratified sampling method whereby they were stratified according to the different residents' committees. Residents were free to decide whether to join the study or not. Written consent was obtained from each participant. The study conformed to the requirements of the *Declaration of Helsinki* and was approved by the Ethics Committee of Peking University First Hospital (approval number 2009-168). A total of 1270 participants initially agreed to take part in the study. Inclusion criteria: 1) Residents of Shichahai community; 2) Duration of residence ≥ 3 years; 3) Age ≥ 35 years. Exclusion criteria: 1) Any respiratory disease besides COPD and asthma including, ① Respiratory system tumor, ② Interstitial lung disease, ③ Bronchiectasis, ④ Lobectomy or pneumonectomy for any reason; 2) Diseases that might influence inflammatory biomarkers; 3) Any chronic infection including, ① active tuberculosis, ② Autoimmune diseases; 4) Severe heart, renal, hepatic, or mental diseases. Following recruitment, appointments were made by telephone for participants to visit the nearest residents' committee to complete questionnaires, lung function tests, and exhaled breath condensate (EBC) collection. At this stage, 1261 participants completed the questionnaires and lung function tests. A total of 1003 participants met our criteria and were selected for the participation. We aimed to analyze the relationship between home-road distance and respiratory indices including lung function, airway inflammation markers, and the prevalence of respiratory symptoms and diseases in all participants. At the follow-up about 3 years later, 398 participants had second lung function tests. In this group, we analyzed the relationship between home-road distance and lung function decline rate.

Questionnaires

At the beginning of the study, each participant was invited to complete a questionnaire requesting basic information, home address, education, income level, occupational exposure, smoking history, chronic respiratory symptoms during the past year, including cough and shortness of breath, and past medical history. Chronic cough was defined as cough lasting for more than 8 weeks in the past year.^[8]

Exposure assessment

Shichahai Community is located at the center of Beijing and contains about 100,000 residents in 5.8 km². There are six major roads across the area. Home-road distance was defined as the distance from the home address to the nearest major road, measured using AMAP 2.0 (AutoNavi Software Co., Ltd., Beijing, China). As previous research has indicated that the concentration of air pollutants drops to background level at 100–300 m from major roads,^[9] and most of our participants lived within 300 m from the major roads, we divided the distance into three categories: 1, <100 m; 2, 100–200 m; and 3, >200 m.

Lung function tests

Lung function was measured using the portable spirometer COPD-6 (Vitalograph Ltd., County Clare, Ireland). The FEV1 and forced expiratory volume in 6 s (FEV6) of each participant were measured three times at intervals of several minutes. The reading with the maximum sum of FEV1 and FEV6 was chosen as the final result. The percentage of the predicted value was calculated. About 3 years later, participants were called for a second lung function test so that the FEV1 decline rate could be assessed.

Exhaled breath condensate collection and measurement

EBC was collected according to the European Respiratory Society/American Thoracic Society recommendations,^[10] using a Chinese-made EBC collector (Converge-Sci Co., Ltd., Beijing, China). In brief, each participant was asked to breathe through a mouthpiece into a condensing tube for 10 min while wearing a nose clip. The temperature of the tube chamber was -20°C . One-way valves were used to avoid rebreathing. Once collected, EBC was deaerated with argon immediately for gas standardization.^[11–13] The pH was then measured immediately using an FE20 pH meter (Mettler-Toledo, Columbus, USA) with an accuracy of ± 0.01 pH. The remaining samples were stored at -80°C for further testing. EBC interleukin 6 (IL-6) levels were tested using Human IL-6 ELISA kits (BMS213/2TEN, Bender Medsystems, Austria). Participants with acute respiratory infection had their EBC collection postponed until 2 weeks after recovery.

Statistical analysis

IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, USA) was used for statistical analysis. When comparing baseline data between the three distance categories, we used one-way analysis of variance (ANOVA) for normally distributed data, the Kruskal-Wallis *H*-test for nonnormally distributed data, and Chi-square tests for binary variables. For regression analysis, we used the distance category number to represent home-road distance and adjusted for potential cofactors that might influence lung function and respiratory condition, including age, gender, body mass index (BMI), smoking status, cumulative cigarette dose, occupational exposure, education, and income level. Multivariate linear regression and logistic regression analyses were used to assess the impact of distance on lung function and respiratory symptoms, respectively. As the EBC pH and IL-6 data were

not normally distributed, Spearman rank correlations were used. $P < 0.05$ was considered statistically significant. Data with normal distribution were presented as mean \pm standard deviation (SD) while data not normally distributed were presented as median (interquartile range, IQR).

RESULTS

The baseline characteristics of the different distance categories are shown in Table 1. A total of 1003 participants were included in this analysis. There were 437, 263, and 303 participants in categories 1, 2, and 3, respectively. No significant difference in baseline characteristics was found between the three groups. The median duration of living at the current address was 28.0 years. There were higher proportions of female and nonsmoking participants.

Lung function

A total of 1003 participants completed the test in 2009. The results are shown in Table 2 and Figure 1.

Multivariate linear regression showed that after adjusting for cofactors mentioned above, shorter distance was associated with lower percentage of predicted value of FEV1 (FEV1% -1.54 , 95% confidence interval [CI]: -0.20 to -2.89). Percentage of predicted value of FEV6 (FEV6%) and FEV1/FEV6 also had an increasing trend with the increase of distance, but the regression analysis showed no statistical significance [Figure 1b and 1c].

Only 398 (39.68%) participants performed a second lung function test about 3 years later (mean 2.6 ± 1.2 years). The annual decline of FEV1 for each category is shown

in Table 2 and Figure 1d. We adjusted for baseline FEV1, as well as for the cofactors mentioned above. The results revealed no significant association between the decline of FEV1 and home-road distance. Factors associated with faster FEV1 decline were older age, female gender, and a history of smoking.

Respiratory symptoms

The prevalence of chronic cough is shown in Table 2. Logistic regression analysis showed that categories 1 and 2 had odds ratios of 2.54 (95% CI: 1.57–4.10) and 1.97 (95% CI: 1.16–3.37) for chronic cough, respectively, compared with category 3 [Figure 2]. No association was found between shortness of breath and the distance category.

Of the 156 participants with chronic cough, 37 (23.7%) had obstructive dysfunction defined as FEV1/FEV6 $<70\%$ and 13 (8.3%) had a history of asthma. Participants with chronic cough had a significantly lower FEV1% (mean 80.06 vs. 94.03, $P < 0.001$) and EBC pH (median 7.75 vs. 7.91, $P = 0.022$) compared with those without.

Exhaled breath condensate inflammation markers

We collected EBC samples from 946 participants. Of these, 301 were <0.5 ml, which was insufficient for pH measurement; hence, a total of 645 pH values were obtained. A subset of 412 samples was chosen for IL-6 measurement.

EBC pH was positively correlated with the distance (rank correlation coefficient of Spearman [r_s] = 0.176, $P < 0.001$), while EBC IL-6, although negatively correlated with EBC pH, was not significantly correlated with distance [Table 3].

Table 1: Baseline characteristics of participants with a home-road distance of <100 m, 100–200 m, or >200 m

Variables	Total ($n = 1003$)	<100 m ($n = 437$)	100–200 m ($n = 263$)	>200 m ($n = 303$)	Statistical values	P
Age (years), mean \pm SD	57.96 \pm 8.99	58.14 \pm 9.14	57.83 \pm 9.00	57.81 \pm 8.80	0.155*	0.857
Male, n (%)	312 (31.1)	138 (31.6)	79 (30.0)	95 (31.4)	0.194†	0.907
BMI (kg/m ²), mean \pm SD	25.51 \pm 3.55	25.38 \pm 3.49	25.65 \pm 3.51	25.57 \pm 3.67	0.551*	0.576
Percentage of smokers, n (%)	279 (27.8)	114 (26.1)	68 (25.9)	97 (32.0)	3.812†	0.149
Pack-years (for smokers), median (IQR)	20.0 (30.0)	20.0 (25.0)	21.0 (26.5)	23.0 (36.5)	4.114†	0.128
Education level, n (%)						
Primary school	127 (12.7)	59 (13.5)	33 (12.5)	35 (11.6)	0.010†	0.995
Middle school	392 (39.2)	161 (36.8)	103 (39.2)	128 (42.2)		
High school	369 (36.7)	171 (39.1)	99 (37.6)	99 (32.7)		
Junior college	87 (8.6)	35 (8.0)	20 (7.6)	32 (10.6)		
University	28 (2.8)	11 (2.5)	8 (3.0)	9 (3.0)		
Monthly income (RMB, Yuan), n (%)						
<1000	28 (2.8)	11 (2.5)	4 (1.5)	13 (4.3)	5.793†	0.055
1000–1999	83 (8.2)	37 (8.5)	21 (8.0)	25 (8.3)		
2000–2999	562 (55.7)	240 (54.9)	141 (53.6)	181 (59.7)		
3000–3999	303 (30.1)	133 (30.4)	93 (35.4)	77 (25.4)		
≥ 4000	27 (2.7)	16 (3.7)	4 (1.5)	7 (2.3)		
Duration of residence (years), median (IQR)	28.0 (20.0)	30.0 (20.0)	25.0 (22.3)	27.0 (26.3)	2.849†	0.241

Data are presented as mean \pm SD, median (IQR) or n (%). * F value; † χ^2 value. Monthly income is shown as renminbi (RMB, Yuan)/person. No significant difference was found between the three groups. BMI: Body mass index; IQR: Interquartile range; SD: Standard deviation.

Table 2: Lung function, respiratory symptoms and diseases of participants with a home-road distance of <100 m, 100–200 m, or >200 m

Distance categories	Lung function						
	<i>n</i>	FEV1 (L)	FEV1%	FEV6 (L)	FEV6%	FEV1/FEV6 (%)	FEV1/FEV6 <70%, <i>n</i> (%)
<100 m	437	2.22 ± 0.60	90.91 ± 18.19	2.79 ± 0.73	93.90 ± 17.67	79.84 ± 9.07	54 (12.4)
100–200 m	263	2.20 ± 0.62	91.37 ± 18.06	2.75 ± 0.78	94.22 ± 19.02	80.40 ± 9.36	21 (8.0)
>200 m	303	2.21 ± 0.61	93.65 ± 20.56	2.74 ± 0.73	95.47 ± 18.06	80.99 ± 9.85	30 (9.9)
Total	1003	2.21 ± 0.61	91.86 ± 18.93	2.76 ± 0.74	94.50 ± 18.21	80.33 ± 9.39	105 (10.5)
Statistical values	-	0.047*	2.002*	0.400*	0.703*	1.384*	3.498†
<i>P</i>	-	0.954	0.136	0.670	0.495	0.251	0.174

Distance categories	Respiratory symptoms and diseases, <i>n</i> (%)			Decline of FEV1 (ml/year)	
	Chronic cough	Shortness of breath	History of asthma	<i>n</i>	Median (IQR)
<100 m	84 (19.2)	84 (19.2)	16 (3.7)	180	22 (98.0)
100–200 m	42 (16.0)	35 (13.3)	5 (1.9)	118	43 (113.0)
>200 m	30 (9.9)	63 (20.8)	8 (2.6)	100	49 (112.5)
Total	156 (15.6)	182 (18.2)	29 (2.9)	398	36 (114.3)
Statistical values	11.883†	5.194†	1.909†	-	5.789†
<i>P</i>	0.003	0.052	0.385	-	0.055

Data are presented as mean ± SD, median (IQR) or *n* (%). **F* value; † χ^2 value. Multivariate linear regression showed that FEV1% decreased 1.54 (95% *CI*: 0.20–2.89) from a further category to a closer category, adjusted for age, gender, BMI, smoking status, smoking pack-years, occupational exposure, education, and income level. Logistic regression analysis showed that shorter home-road distance was an independent risk factor for chronic cough, adjusted for age, gender, BMI, smoking status, smoking pack-years, occupational exposure, education, and income levels. Compared with category 3, odds ratios for categories 1 and 2 were 2.54 (95% *CI*: 1.57–4.10) and 1.97 (95% *CI*: 1.16–3.37), respectively. FEV1: Forced expiratory volume in 1 s; FEV6: Forced expiratory volume in 6 s; FEV1%: Percentage of predicted value of FEV1; FEV6%: Percentage of predicted value of FEV6; SD: Standard deviation; IQR: Interquartile range; *CI*: Confidence interval; -: No data; BMI: Body mass index.

Of the relationships between EBC biomarkers and lung function, only EBC pH was positively correlated with FEV1% ($r_s = 0.097$, $P = 0.014$). Neither EBC pH nor IL-6 was correlated with FEV1 decline.

DISCUSSION

In this study of a cohort of residents in Beijing, we revealed that living near a major road is associated with lower FEV1%, a higher prevalence of chronic cough, and lower EBC pH values. These results support our hypothesis that traffic-related air pollution causes airway inflammation and results in respiratory symptoms and lung function decline.

The Swiss Cohort Study on Air Pollution and Lung and Heart Disease in Adults^[14] and the European Study of Cohorts for Air Pollution Effects^[15] are two large cohort studies that revealed lower lung function in severely polluted air. In addition to the concentration of air pollutants, several studies^[2–5] have used home-road distance as an indicator of pollution exposure. Most of these studies have suggested that distance from a major road is positively associated with lung function. The study used the same indicator for exposure and showed similar results in a city with much heavier traffic and air pollution. In a Swedish study by Carlsen *et al.*,^[3] major roads with heavy traffic were defined as >10,000 vehicles/day and very heavy traffic as >30,000 vehicles/day. The six major roads in this study had much higher traffic flow, of which two had traffic burdens exceeding 100,000 vehicles/day. Although there was lower proportion of smokers in our cohort than in the Swedish

cohort, ours had lower FEV1% and a greater decline in FEV1% the closer to a major road. Although it is difficult to compare results from different studies, this might be due to higher air pollution levels near major roads in Beijing.

We used FEV6, which has been demonstrated to be an alternative parameter of forced vital capacity (FVC),^[16] combined with FEV1, to evaluate airflow obstruction. The percentage of predicted value was used for analysis as it adjusts for age, gender, and height. Of all the lung function parameters, only FEV1% was correlated with the home-road distance, indicating that FEV1% might be the most sensitive measure of air pollution exposure.

As mentioned earlier, Rice *et al.*^[4] found a faster decline in FEV1 and FVC in people living closer to a major road. However, we failed to observe this trend. In our study, only a smoking history, older age, and female gender were positively correlated with FEV1 decline rate, which have also been reported in other studies.^[17,18] Rice *et al.*^[4] had a sample size of more than 6000 and a follow-up period of 4 years, while this study was limited by a small sample size and loss to follow-up, limiting clarification of this issue. The correlation between home-road distance and lung function decline rate needs further well-designed studies for confirmation.

Most of the participants with chronic cough had no history of respiratory diseases. A previous study in China found a correlation between the concentration of air pollutants in different areas and the prevalence of chronic cough in children.^[19] However, as participants in this study were from

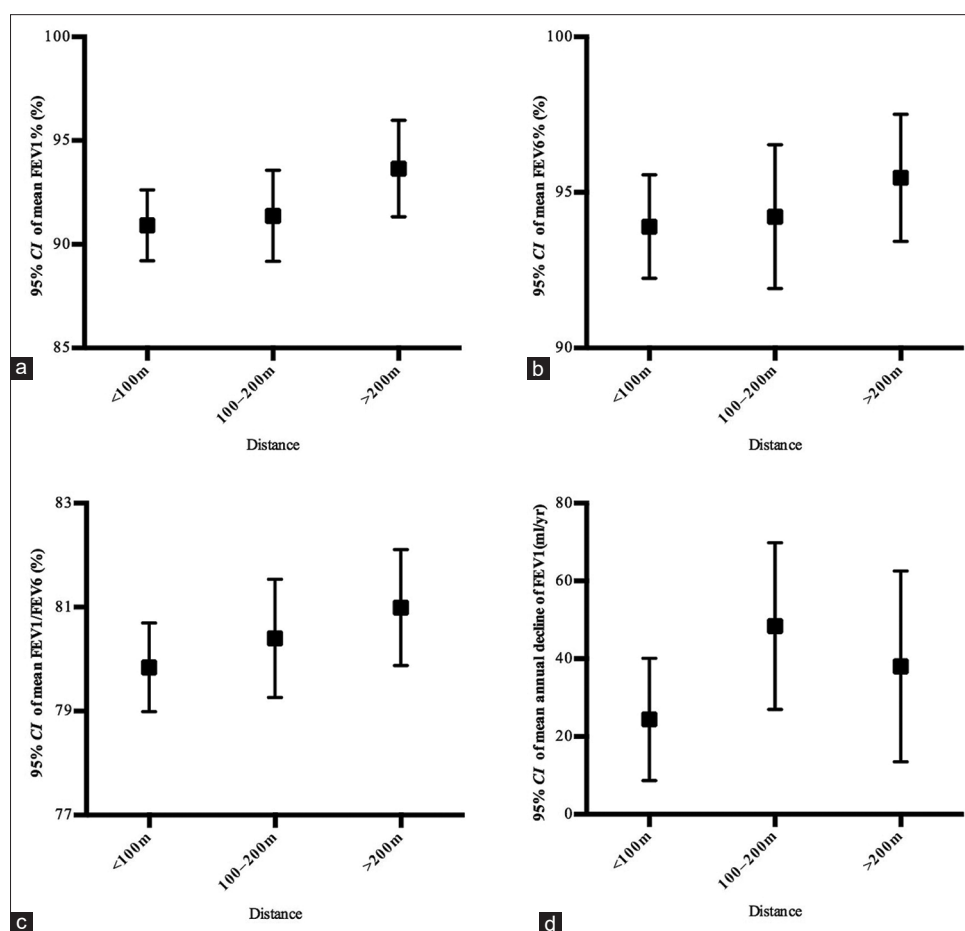


Figure 1: Lung function of participants with a home-road distance of <100 m, 100–200 m, and >200 m. (a-c) FEV1%, FEV6%, and FEV1/FEV6 all demonstrate an increasing trend with longer distance. (d) No clear trend can be seen in the annual decline of FEV1 (ml/year) with increased distance. Distance: Home-road distance; FEV1%: Percentage of predicted value of forced expiratory volume in 1 s; FEV6%: Percentage of predicted value of forced expiratory volume in 6 s; CI: Confidence interval.

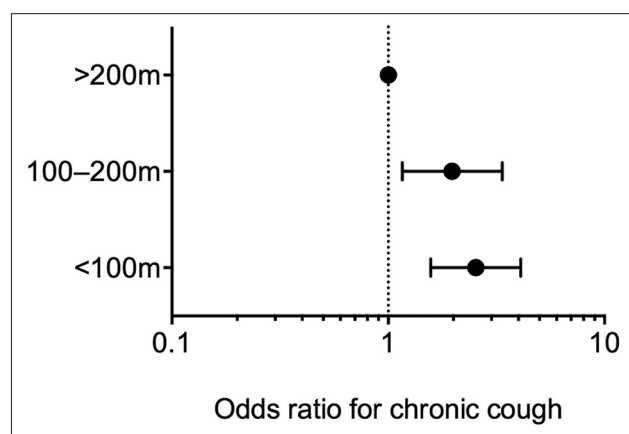


Figure 2: Odds ratio for chronic cough for participants with a home-road distance of <100 m, 100–200 m, or >200 m. Compared with participants with a home-road distance of >200 m, participants with a home-road distance of <100 m or 100–200 m had a higher prevalence of chronic cough, with an odds ratio of 2.54 (95% CI: 1.57–4.10) and 1.97 (95% CI: 1.16–3.37), respectively. Chronic cough was defined as cough that lasted for more than 8 weeks during the past year. CI: Confidence interval.

different areas of the country, potential cofactors could have biased the results. An Italian study assessed the relationship

Table 3: EBC pH and IL-6 of participants with a home-road distance of <100 m, 100–200 m, or >200 m

Distance categories	EBC pH		EBC IL-6 (pg/ml)	
	n	Median (IQR)	n	Median (IQR)
<100 m	280	7.80 (0.63)	153	7.77 (5.19)
100–200 m	163	7.78 (0.63)	155	8.55 (6.38)
>200 m	202	8.08 (0.52)	104	7.04 (7.00)
Total	645	7.87 (0.63)	412	7.84 (6.08)
χ^2	-	36.204	-	3.961
P	-	0.000	-	0.138

Data are shown as median (IQR). Spearman's correlation test showed that EBC pH was positively correlated with home-road distance (rank correlation coefficient of Spearman [r_s] = 0.176, $P < 0.001$). EBC: Exhaled breath condensate; IL-6: Interleukin 6; IQR: Interquartile range; -: No data.

between chronic cough in children and home-road distance, but got a negative result.^[20] In our study, we found living near a major road to be an independent risk factor of chronic cough in adults, perhaps due to a higher concentration of pollutants in the near-road area in our study. As various studies have found that airway inflammation is initiated after air pollution exposure,^[7,21,22] it is reasonable to suggest that airway inflammation might be related to chronic cough. In fact, the

lower pH in participants with chronic cough in this cohort supports this hypothesis. Niimi *et al.*^[23] also found lower EBC pH in chronic cough participants, independent of the cause. They hypothesized that protons in the airway lining fluid might activate the cough reflex. With the retrospective nature of our study, we were not able to exclude gastroesophageal reflux disease and upper airway cough syndrome, which have also been found to be common reasons for chronic cough in China.^[24] Further investigation is needed to confirm the relationship between air pollution and chronic cough.

EBC pH has been reported to be a reproducible index for lower airway acidity,^[25] with lower EBC pH correlated with various airway inflammation biomarkers.^[13] Therefore, EBC pH serves as a good indicator of airway inflammation. De Prins *et al.*^[21] found that black carbon exposure lowers EBC pH in children. Studies in adults^[26-28] have also found negative correlations between air pollution exposure and EBC pH. The study observed more evident airway acidification in participants exposed to traffic pollution, adding to the evidence that air pollution results in airway inflammation.

Papaioannou *et al.*^[29] reported that EBC pH was lower in global initiative for chronic obstructive lung disease (GOLD) Stage III and IV COPD patients compared with GOLD Stage I and II patients. Other than this, there appear to be no reports of a correlation between EBC pH and lung function. In this study, lower EBC pH was correlated with higher FEV1%. Therefore, EBC pH seems to be a potential biomarker for air pollution exposure and its adverse effects. EBC IL-6, on the other hand, was not correlated with pollution exposure. As the mechanism of airway inflammation caused by air pollution is not clear, additional biomarkers should be investigated in the future studies.

Several studies^[5,30-34] have indicated a higher incidence of COPD and asthma in participants with higher air pollution exposure, most of them with limited or inconclusive evidence. The complexity of air pollution exposure evaluation and control of cofactors make such studies quite difficult. We found a higher proportion of airflow obstruction and asthma in category 1, but this was not statistically significant. We studied the prevalence, rather than the incidence, of airway diseases, which limits the conclusions we can make regarding airway diseases. We aimed to analyze the prevalence of asthma as a result of air pollution exposure. However, if asthma existed before the exposure, it might have biased the results of lung function and airway inflammation markers. Thus, we are reluctant to draw any conclusions in regard to home-road distance and airway diseases. However, with lower EBC pH, lower FEV1%, and a higher prevalence of chronic cough in the shorter distance category, we believe that participants in category 1 might have a higher risk of developing airway diseases and this needs further investigation.

This study has several limitations: the small sample size and short follow-up period make it difficult to assess differences in lung function decline rate and prevalence of airway diseases in different distance categories, and to adjust for cofactors.

We used the distance from the nearest major road as the indicator for traffic-related air pollution exposure. As the concentration of near-roadway particles drops quickly with distance from the road, within about 100–300 m, by categorizing the home-road distance, this study obtained a gradient to assess local pollution exposure in an urban environment. However, as major roads in the central district of Beijing are near each other, many participants were exposed to traffic exhaust from more than one road. The distance from only the nearest road might not be accurate enough to represent the true exposure.

Another limitation was that 301 EBC samples contained <0.5 ml of EBC, which was insufficient for the measurement of pH values. The loss of these data might have biased the results. A longer collection time should have been used for these 301 participants to obtain more EBC. For the IL-6 measurement, 412 EBC samples were chosen. We believe that this is unlikely to have biased the results, as when we compared the baseline characteristics of the 412 participants in the <100 m, 100–200 m, and >200 m groups, they did not differ significantly.

As most of our participants had been living for many years in their current addresses, the background air pollution exposure seemed unlikely to differ between participants. Work exposure and outdoor activities were not considered in our study, which is also a limitation. However, most of the participants were elderly people who were retired. Even in relatively younger participants, workplace exposure was unlikely to differ between the three groups. Hence, we conclude that the exclusion of these considerations is unlikely to bias the results.

Overall, this study suggests that lower FEV1%, airway acidification, and chronic cough in Beijing residents are associated with long-term exposure to traffic-related air pollution, using home-road distance as the indicator. EBC pH was also related to FEV1% and might serve as a potential biomarker for air pollution exposure and its adverse effects on the respiratory system.

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Conflicts of interest

There are no conflicts of interest.

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