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Reduced ambient $PM_{2.5}$, better lung function, and decreased risk of chronic obstructive pulmonary disease

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ABSTRACT

Background: Several studies reported that long-term exposure to fine particulate matter ($PM_{2.5}$) was associated with an increased risk of chronic obstructive pulmonary disease (COPD). It remains unclear whether reduced $PM_{2.5}$ can decrease the risk of COPD development.
Objective: To investigate the associations of dynamic changes (including deterioration and improvement) in long-term exposure to ambient $PM_{2.5}$ with changes in lung function and the incidence of COPD.
Methods: A total of 133,119 adults (aged 18 years or older) were recruited in Taiwan between 2001 and 2014. All participants underwent at least two standard medical examinations including spirometry test. We estimated $PM_{2.5}$ concentrations using a high-resolution (1 km^2) satellite-based spatio-temporal model. The change in $PM_{2.5}$ ($\Delta PM_{2.5}$) was defined as the difference in concentration of $PM_{2.5}$ between the respective visit and the previous visit. We used a multivariable mixed linear model and time-varying Cox model to investigate the associations of change in $PM_{2.5}$ with annual change of lung function and the incidence of COPD, respectively.
Result: The $PM_{2.5}$ concentration in Taiwan increased during 2002–2004 and began to decrease around 2005. Every 5-$\mu g/m^3$/year decrease in the annual change of $PM_{2.5}$ (i.e., $\Delta PM_{2.5}$/year of 5 $\mu g/m^3$/year) was associated with an average increase of 19.93 mL/year (95 %CI: 17.42,22.43) in forced expiratory volume in 1 s (FEV_1), 12.76 mL/year (95 %CI: 9.84,15.66) in forced vital capacity (FVC), 70.22 mL/s/year (95 %CI: 64.69,76.16) in midexpiratory flow between 25 and 75% of the forced vital capacity (MEF25-75), 0.27%/year (95 %CI: 0.21%, 0.32%) in FEV_1/FVC/year. Every 5 $\mu g/m^3$ decrease in $PM_{2.5}$ (i.e., $\Delta PM_{2.5}$ of 5 $\mu g/m^3$) was associated with a 12% (95 %CI: 7%, 17%) reduced risk of COPD development. The stratified and sensitivity analyses generally yielded similar results.
Conclusion: An improvement in $PM_{2.5}$ pollution exposure was associated with an attenuated decline in lung function parameters of FEV_1, FVC, MEF25-75, and FEV_1/FVC, and a decreased risk of COPD development. Our findings suggest that strategies aimed at reducing air pollution may effectively combat the risk of COPD development.

1. Introduction

The World Health Organization (WHO) recently announced that more than 90% of the global population resides in areas where the air quality exceeds the WHO limits (WHO, 2020). Air pollutants have been considered as the largest single environmental risk and a leading

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contributor to the global disease burden. In 2016, 4.2 million deaths worldwide were attributed directly to ambient air pollution (WHO, 2020).

Recognizing air pollution as a critical risk factor affecting public health, many countries have implemented strategies to combat this risk. The concentration of air pollutants in many parts of the world, especially in the economically developed regions, have experienced dynamic increases and decreases over the past few decades. It is crucial to document whether past efforts to reduce air pollution have yielded demonstrable improvements in public health and to better predict whether future efforts will continue to do so.

Our previous studies (Guo et al., 2018; Guo et al., 2019) and others (Rice et al., 2015; Liu et al., 2017; Wang et al., 2018; Usemann et al., 2019) have reported that chronic exposure to air pollutants, especially particulate air pollution, was associated with a decrease in lung function in both children and adults, and an increase in the risk of chronic obstructive pulmonary disease (COPD) in adults. Previous study demonstrated that multiple lung function trajectories may lead to COPD, including reduced lung growth leading to low maximally attained lung function, and accelerated lung function decline (McGeachie et al., 2016). Air pollution may thus be an important contributor to the development of COPD, which was the 6th leading drivers of increasing burden of disability-adjusted life-years (DALYs) globally and accounts for 74 million DALY in 2019 (GBD 2019 Diseases and Injuries Collaborators, 2020). It is crucial to determine whether reduced air pollution may improve lung health and lead to a decrease in the incidence of COPD. Such information may motivate changes in public policy to a greater extent than the demonstration of associations between bad air and poor pulmonary health. However, such data is limited and most previous studies were focused on children (Heinrich et al., 2000; Bayer-Oglesby et al., 2005; Gauderman et al., 2015) and lung function (Huls et al., 2019; Schikowski et al., 2013; Downs et al., 2007; Boogaard et al., 2013). There is limited evidence about the beneficial health effect of air quality improvement on COPD development.

The ambient $PM_{2.5}$ concentration in Taiwan peaked in approximately 2005 and has been declining since then. This provides us a good backdrop for a "natural experiment" to examine the potential beneficial health effects of air quality improvement on COPD development. We therefore conducted a longitudinal cohort study to investigate the association between dynamic changes in long-term exposure to ambient $PM_{2.5}$ ($\Delta PM_{2.5}$), changes in lung function parameters [i.e. changes in forced expiratory volume in the first second/years (ΔFEV_1/years), changes in forced vital capacity/years (ΔFVC/years), changes in mid-expiratory flow between 25 and 75% of the forced vital capacity/year (ΔMEF25-75/years), and changes in the ratio of FEV_1 and FVC (ΔFEV_1/FVC/years)] and the risk of COPD development in 133,119 adults in Taiwan.

2. Methods

2.1. Study population

The participants were from an ongoing longitudinal cohort, which has been documented in detail elsewhere (Guo et al., 2018; Zhang et al., 2018; MJ Health Research Foundation, 2016). In short, the MJ Health Management Institution has been providing a standard medical screening programme for Taiwan residents since 1994. Participants who purchased the memberships were encouraged to visit the institution periodically for a series of medical examinations. These included anthropometric measurements, spirometry tests, blood and urine tests and imaging analyses, as well as a standard self-administered questionnaire survey. These data have been digitised since 1996 and more than 0.5 million participants were recruited between 1996 and 2014. The cohort members were Taiwan residents who come from all over the country. The median age and sex ratio of the screening participants were similar to those of the Taiwan population in 2010, which was approximately the median year of enrollment (2001–2014) [the median age was 38 years in this cohort members vs. 37.2 years in the total population of Taiwan (Elaboration of data by United Nations, 2019), whilst the sex ratio (female = 100) was 0.93 in the cohort members vs. 1.01 in the general population of Taiwan (National Bureau of Statistics of China, 2019)]. All participants have signed informed consent to authorise the use of their data for research prior to undergoing the medical examinations during each visit. The Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee approved this study.

The detailed process of participant selection is shown in Fig. S1. Initially, we recruited 422,013 adults aged 18 years or older from 2001 to 2014 when the assessment of ambient $PM_{2.5}$ was available. Subsequently, 234,767 participants were excluded because they only have one medical visit, 54,127 participants were further excluded due to: missing information on height or weight (n = 215), lifestyle factors or educational level (n = 19,418), lung function (n = 28,706), and lung cancer or asthma at baseline (n = 5,788).

As a result, 133,119 participants residing in sixteen municipalities or cities of Taiwan [i.e., Taipei, Keelong, Taoyuan, Hsinchu, Ilan, Miaoli, Taichung, Changhua, Nantou, Hualien, Yunlin, Chiayi, Tainan, Kaoshiung, Taitung and Pingtung (the municipalities/cities locations in Taiwan are shown in Fig. S2)] were included to investigate the association between $\Delta PM_{2.5}$/year and change in lung function (i.e., ΔFEV_1/year, ΔFVC/year, ΔMEF25-75/year, and ΔFEV_1/FVC/year). Of the 133,119 participants, 2,003 participants with COPD at baseline (defined as $FEV_1/FVC < 70\%$ or self-report of physician-diagnosed COPD) were further excluded, and the remaining 131,116 participants were used to investigate the association between $\Delta PM_{2.5}$ and incident COPD.

2.2. Ambient $PM_{2.5}$ assessment

The detailed method of $PM_{2.5}$ exposure estimation has been described in our previous studies (Guo et al., 2018; Zhang et al., 2017; Lin et al., 2015). A satellite-based spatial–temporal model with a spatial resolution of 1 km^2, which used the aerosol optical depth (AOD) data derived from Moderate Resolution Imaging Spectroradiometer carried on U.S. National Aeronautics and Space Administration satellite, was used to assess the ground-level $PM_{2.5}$. The model was validated by comparing the monitoring $PM_{2.5}$ data from more than 70 monitoring stations across Taiwan with the estimated $PM_{2.5}$ exposure. The correlation coefficients between the monitored and modelled annual average $PM_{2.5}$ ranged from 0.79 to 0.83.

Each participant's mailing address was collected during each medical visit so that the medical reports could be delivered to them. During the follow-up period, 39,215 (29.5%) participants changed their addresses and the data analysis accounted for the changes. The addresses were geocoded to yield latitude and longitude data so that the address-specific yearly average $PM_{2.5}$ concentrations could be estimated. The 2-year average $PM_{2.5}$ concentration was used as the indicator of long-term exposure to $PM_{2.5}$ and it was calculated based on the concentrations from the year of and the year before the medical examination. According to previous publications (Bayer-Oglesby et al., 2005; Downs et al., 2007; Laden et al., 2006; Schindler et al., 2009). The change of $\Delta PM_{2.5}$ (i.e., $\Delta PM_{2.5}$) was defined as difference in concentration of $PM_{2.5}$ between the respective visit and the previous visit. A negative value from this calculation represented an improvement in the $PM_{2.5}$ air quality.

2.3. Outcome ascertainment

The health outcomes for this study were incident COPD and annual change of lung function (i.e., ΔFEV_1/year, ΔFVC/year, ΔMEF25-75/year, ΔFEV_1/FVC/year).

As our previous publication depicted (Guo et al., 2018), the spirometry was performed by trained professionals using MICROSPIRO HI-501 (Fällanden, Switzerland) or CHESTGRAH HI-701 (Chest M.I.

Tokyo, Japan), while participants were in a standing position. The procedures strictly followed the protocol of the American Thorax Society (Miller et al., 2005). All participants were required to blow at least three times, at least twice of which could be reproducible within 5% of both FVC and FEV_1. FVC and FEV_1 scores came from the maximum curve, while MEF25-75 score came from the best curve (defined as the maximum sum of FEV_1 and FVC) for subsequent reports and current data analysis.

The annual change of lung function (i.e., ΔFEV_1/year, ΔFVC/year, ΔMEF25-75 /year, ΔFEV_1/FVC/year) was defined as difference in lung function (i.e., FEV_1, FVC, MEF25-75, FEV_1/FVC) between the respective visit and the previous visit divided by the time in years between the two visits. A negative value indicates a decline in the respective parameter of lung function over time.

After the baseline assessment at the first visit, The 131,116 participants without COPD were followed up and the incident COPD was identified by spirometry test during subsequent medical assessment [defined as a ratio of FEV_1/FVC < 70% based on the Global Initiative for COPD (Pauwels et al., 2012; Global Initiative for Chronic Obstructive Lung Disease, 2016), or as a self-report of physician-diagnosed COPD]. The entry date was defined as the time of recruitment (i.e. the baseline medical examination), while the date of study exit was set as the date of the first occurrence of COPD or the date of the last visit if COPD did not occur.

2.4. Covariates

Information on participants' demographic characteristics, lifestyle factors, and medical history were collected by a standard self-administered questionnaire. Height and weight were measured using an anthropometer (kn-5000a, nakamura, Tokyo, Japan) with participants wearing light indoor clothing and no shoes. Body mass index (BMI) was calculated according to the following equations: BMI (kg/m^2) = body weight (kg)/height squared (m^2).

2.5. Statistical analysis

All statistical analyses were conducted using R 3.3.2. (R Core Team, Vienna, Austria), and two-sided *P* values < 0.05 were considered statistically significant.

For the association between change in $PM_{2.5}$ and annual change of lung function, the multivariable mixed linear models with random participant intercepts were adopted. The annual change of $PM_{2.5}$ (i.e., $\Delta PM_{2.5}$/year, defined as difference in concentration of $PM_{2.5}$ between the respective visit and the previous visit divided by the time in years between the two visits) was adopted as exposure variable, considering that change in lung function was measured as mean annual change. All information except for vital status was repeatedly collected at each medical visit. Thus, $\Delta PM_{2.5}$/year and all covariates (except for sex) were treated as time-dependent variables in the data analysis to account for the changes of these variables during the study period. Covariates were selected a priori, mainly based on literature review (Guo et al., 2018; Rice et al., 2015; Liu et al., 2017; Wang et al., 2018; Adam et al., 2015; Wang et al., 2019). The city-level random intercept was used to control for within-city clustering effects based on the participants' addresses. In addition to treating $\Delta PM_{2.5}$/year as a continuous variable, we also categorized $\Delta PM_{2.5}$/year into tertiles and selected the second tertile (i.e., the smallest change) as the reference group for comparing the effects of air quality deterioration and improvement. Four models were developed: Model 1 was not adjusted. Model 2 was adjusted for age (years), sex (male or female), educational level (<10, 10–12 years, 13–16 or > 16 years), and BMI (kg/m^2, continuous). Model 3 further adjusted for smoking (never, former or current), alcohol use (<1, 1–3 or > 3 times/week), physical activity (defined as the product of the metabolic equivalent value [MET = 1 kcal/h per kg body weight] and duration of exercise [hours] as inactive, <3.75; low, 3.75–7.49; medium, 7.50–15.0; high, 15.0–25.49; or very high, ≥25.50 MET-h) (Lao et al., 2018; Physical Activity Guidelines Advisory Committee Report, 2008), fruit intake (<1, 1–2 or > 2 servings/day), vegetable intake (<1, 1–2 or > 2 servings/day), occupational exposure to dust/organic solvents (information was collected by asking the question "are there any occupational hazards in your workplace?" with a list of occupational hazards: yes or no) and season (spring: March to May; summer: June to August; autumn: September to November; or winter: December to February). Model 4 comprised Model 3 plus an adjustment for the $PM_{2.5}$ concentration at baseline.

For the association between change of $PM_{2.5}$ and the incidence of COPD, the time-varying Cox regression model with random participant intercepts was used. The absolute changes in air pollution (i.e., $\Delta PM_{2.5}$, defined as difference in concentration of $PM_{2.5}$ between the respective visit and the previous visit) was used as the exposure variable, because time-to-event has been considered in the Cox model. Again, a city-level random intercept was used to control for within-city clustering effects based on the participants' addresses. The four aforementioned models were adopted to calculated hazard ratio (HR) and 95% confidence interval (CI).

Subgroup analyses were also conducted to investigate whether these associations were modified by sex (men or women), BMI (<25 kg/m^2 or ≥ 25 kg/m^2), smoking status (never, former, or current), and follow up duration (stratified by median, i.e., ≤4.3 years or > 4.3 years). Each potential modifier was examined in a separate model by adding a multiplicative interaction term (i.e., potential modifier * continuous $\Delta PM_{2.5}$).

We also conducted six sensitivity analyses to test the stability of these associations: 1) excluding participants who used company address to eliminate the potential exposure misclassification by different types of addresses; 2) excluding individuals with a history of cardiovascular disease or cancer at baseline to eliminate the potential confounding effects of comorbidity; 3) excluding those with age of 30 years or younger to eliminate the potential effect of lung function growth during 18–30 years; 4) restricting participants who did not move to eliminate the potential effect of moving for health related reasons; 5) Considering the lag effects of air pollution on the risk of COPD development using the yearly average $PM_{2.5}$ concentration before the year of medical examination as the exposure metric because the effect of $PM_{2.5}$ on COPD is a chronic process; 6) we used Global Lung Function Initiative (GLI) 2012 reference values for lower limit of normal (LLN) to define COPD (Quanjer et al., 2012).

3. Results

The general characteristics of study participants are presented in Table 1. Most participants included in the present study were never-smokers, had an education level of college or above, and consume alcohol < 1 time/week.

For the investigation on the association between $\Delta PM_{2.5}$ and annual change of lung function parameters, a total of 133,119 participants (49.7% men) with a mean age of 39.9 ± 12.3 years at baseline were included. The median follow-up duration was 4.3 years [range: 1–13.9 years; interquartile range (IQR): 2.1–7.5 years]. The mean number of medical visits was 3.6 (range: 2–21; IQR: 2–4). The mean interval of the medical visits was 24.7 months (range: 3–166 months; IQR: 12–29 months) with a maximum of 21 follow-up.

For the investigation on the association between $\Delta PM_{2.5}$ and the incidence of COPD, a total of 131,116 participants were included. They had similar distributions as the 133,119 participants described above. During the follow-up period, 2,994 incident cases of COPD were identified.

The spatial distribution of study participants/observations by year is presented in Fig. 1. As demonstrated, the participants generally lived in the western part of the island of Taiwan. The $PM_{2.5}$ concentrations increased in 2002 and 2003, peaked in 2004, and began to decrease in

Table 1
Baseline characteristics of the participants.

	Baseline of included participants[a] (n = 133,119)	Baseline of excluded participants[b] (n = 288,894)	Baseline of non-COPD [c] (n = 131,116)
Age (years)	39.9 (12.3)	39.6 (13.4)	39.7(12.2)
Male	66,098(49.7%)	136,777(47.35%)	65,095 (49.7%)
Education			
High school or lower	48,469(36.4%)	98,972(37.2%)	47,346 (36.1%)
College or university	69,777(52.4%)	135,885(51.0%)	69,064(52. 7%)
Postgraduate	14,873(11.2%)	31,366(11. 8%)	14,706(11. 2%)
Smoking status			
Never	99,535(74.8%)	193,900(73.3%)	98,123 (74.8%)
Former	7,378(5.5%)	15,276(5.8%)	7,224(5.5%)
Current	26,206(19.7%)	55,324(20.9%)	25,769 (19.7%)
Alcohol drinking			
<1 time/week	114,084(85.7%)	219,489(85.8%)	112,375 (85.71%)
1–3 times/week	12,724(9. 6%)	23,900(9.3%)	12,561 (9.58%)
>3 times/week	6,311(4.7%)	12,578(4.9%)	6,180 (4.71%)
Physical activity intensity			
Inactive	65,492(49.2%)	149,962(55.0%)	64,603 (49.27%)
Low	28,227(21.2%)	48,901(18.0%)	27,831 (21.23%)
Moderate	22,775(17.1%)	40,981(15.0%)	22,395 (17.08%)
High	16,625(12.5%)	32,628(12.0%)	16,287 (12.43%)
Occupational exposure (solvent/dust)	10,883(8.2%)	21,190(7.4%)	10,766 (8.21%)
FVC (mL)	2,935(814.3)	2,874(880.9)	2,936.7 (808.9)
FEV_1 (mL)	2,648.1(736.1)	2,579.9(804.8)	2,662.6 (726.2)
MEF25-75 (mL/s)	3,547.3(1161.4)	3,445.1(1273.3)	3,572.8 (1145.3)
FEV_1/FVC ratio (%)	90.5(8.3)	89.9(9.2)	91.0 (7.3)
2-year average $PM_{2.5}$ ($\mu g/m^3$)	26.7(7.8)	26.6 (7.5)	26.7(7.8)
Incident COPD	N/A	N/A	2,994

The statistics are shown as mean (standardized deviation) for continuous variables and count (percentage) for categorical variables, respectively.
[a] Characteristics of the 133,119 participants at baseline.
[b] Characteristics of the 288,894 excluded participants at baseline.
[c] Characteristics of the 131,116 non-COPD participants at baseline.

2005. The values of 2-year average concentrations of $PM_{2.5}$ in Taiwan from 2001 to 2014 are shown in Table S1.

Regarding the association of $\Delta PM_{2.5}$/year and the annual change of lung function parameters (Table 2), participants who were exposure to the 1st tertile of $\Delta PM_{2.5}$ (i.e. improved air quality) had positive coefficients for all parameters comparing with those who were exposure to the 2nd tertile of $\Delta PM_{2.5}$ (the smallest change in $PM_{2.5}$). In contrast, those who were exposure to the 3rd tertile of $\Delta PM_{2.5}$ (i.e., deteriorated $PM_{2.5}$ air quality) had negative coefficients for all parameters. There was an general significantly negative association between annual change in all four parameters (i.e., FEV_1, FVC, MEF25-75, and FEV_1/FVC) and change in $PM_{2.5}$, with an average increase in FEV_1 by 19.93 mL/year (95 %CI: 17.42, 22.43), FVC by 12.76 mL/year (95 %CI: 9.84,15.66), MEF25-75 by 70.22 mL/s/year (95 %CI: 64.69,76.16), and FEV_1/FVC

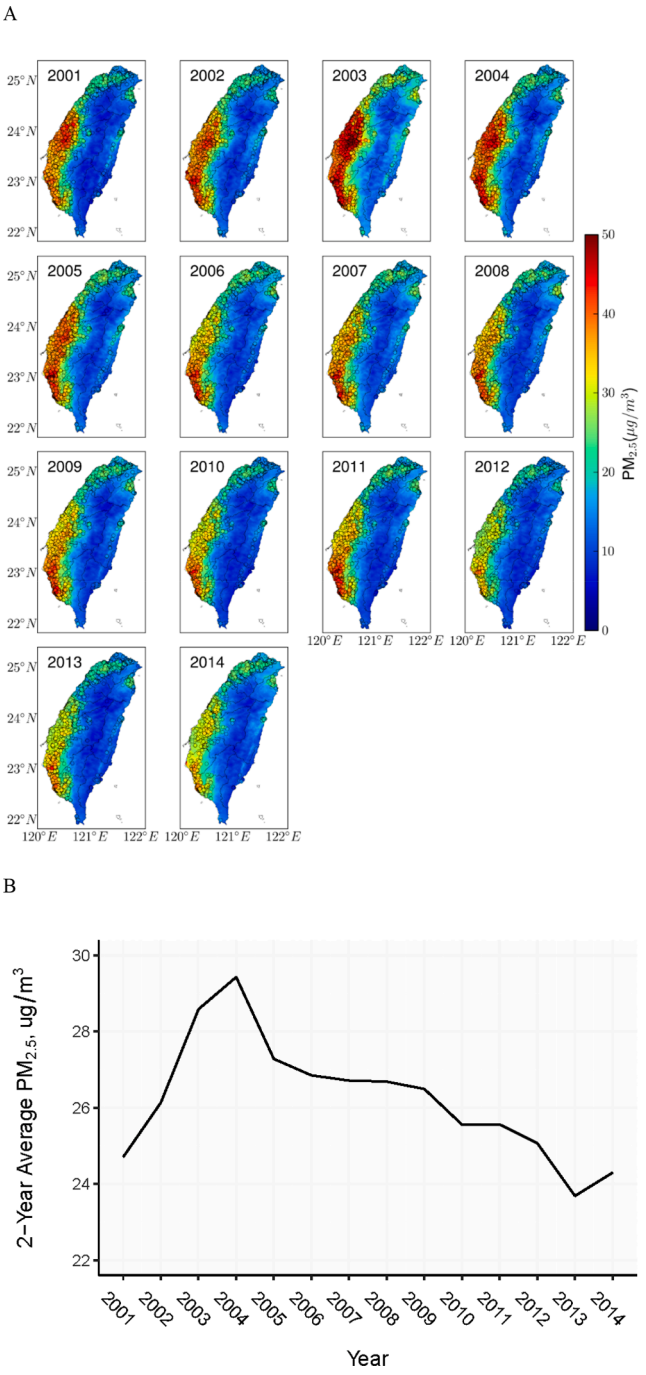

Fig. 1. Maps of the participants' locations and trends in the 2-year average concentrations of fine particulate matter ($PM_{2.5}$) in Taiwan between 2001 and 2014. (A) Locations (circles) of the addresses corresponding to 479,856 observations from the 133,119 participants by year. (B) Trends in the 2-year average concentrations of $PM_{2.5}$ in the 479,856 observations recorded in Taiwan between 2001 and 2014.

by 0.27%/year (95 %CI: 0.21%,0.32%) for each 5 ug/m^3/year improvement in $PM_{2.5}$, respectively.

With Regards to the association between $\Delta PM_{2.5}$ and incident COPD (Table 3), participants with the 1st tertile of $\Delta PM_{2.5}$ (i.e. improved air quality) had a decreased risk of COPD development (HR: 0.75; 95 %CI: 0.68, 0.82) comparing with those who were exposure to the 2nd tertile of $\Delta PM_{2.5}$ (the smallest change in $PM_{2.5}$). But the difference in risk for those with 3rd tertile of $\Delta PM_{2.5}$ (i.e., deteriorated $PM_{2.5}$ air quality) compared to the intermediate category was not statistically significant

Table 2
The association between $\Delta PM_{2.5}$/year and change in lung function.

Models [a]	Model 1		Model 2		Model 3		Model 4	
	Coef (95% CI)	*P*	Coef (95% CI)	*P*	Coef (95% CI)	*P*	Coef (95% CI)	*P*
ΔFEV_1/years (mL/year)								
1st Tertile (−63.28 ~ −0.55)	22.05 (19.69,24.37)		22.05 (19.70, 24.38)		21.68 (19.33, 24.00)		21.87 (19.51, 24.20)	
2nd Tertile (−0.55 ~ 0.23)	Ref		Ref		Ref		Ref	
3rd Tertile (0.23 ~ 35.07)	−6.89 (−9.15,−4.64)		−7.30 (−9.56,−5.04)		−7.46 (−9.72,−5.20)		−7.66 (−9.93, −5.41)	
Trend test [b]		<0.001		<0.001		<0.001		<0.001
Every average 5 μg/m^3/ year decrease	19.81 (17.32, 22.28)		19.65 (17.16, 22.12)		19.60 (17.10, 22.08)		19.93(17.42,22.43)	
ΔFVC/years (mL/year)								
1st Tertile (−63.28 ~ −0.55)	17.75 (15.02,20.46)		17.82 (15.10, 20.53)		17.34 (14.62, 20.05)		17.69 (14.96, 20.41)	
2nd Tertile (−0.55 ~ 0.23)	Ref		Ref		Ref		Ref	
3rd Tertile (0.23 ~ 35.07)	−3.40 (−6.02,−0.78)		−3.95 (−6.57,−1.32)		−3.35 (−6.97,−1.72)		−4.56 (−7.19, −1.92)	
Trend test [b]		<0.001		<0.001		<0.001		<0.001
Every average 5 μg/m^3/ year decrease	12.34 (9.45, 15.22)		12.26 (9.37, 15.14)		12.31 (9.42, 15.19)		12.76 (9.84,15.66)	
ΔMEF25-75/years (mL/s/year)								
1st Tertile (−63.28 ~ −0.55)	56.51 (50.95, 62.04)		56.56 (50.99,62.08)		56.48 (50.91,62.00)		56.61 (51.04,62.15)	
2nd Tertile (−0.55 ~ 0.23)	Ref		Ref		Ref		Ref	
3rd Tertile (0.23 ~ 35.07)	−40.83 (−46.18,−35.49)		−41.65 (−47.01,−36.31)		−40.87 (−46.24,−35.52)		−41.06 (−46.46,−35.71)	
Trend test [b]		<0.001		<0.001		<0.001		<0.001
Every average 5 μg/m^3/ year decrease	71.33 (65.43, 77.21)		70.93 (65.02,76.80)		70.27 (64.35,76.15)		70.22 (64.69,76.16)	
ΔFEV_1/FVC/years (%/year)								
1st Tertile (−63.28 ~ −0.55)	0.18 (0.13,0.24)		0.18 (0.13,0.24)		0.18 (0.13,0.24)		0.19 (0.13,0.24)	
2nd Tertile (−0.55 ~ 0.23)	Ref		Ref		Ref		Ref	
3rd Tertile (0.23 ~ 35.07)	−0.12 (−0.17,−0.07)		−0.11 (−0.16,−0.06)		−0.10 (−0.16,−0.05)		−0.10 (−0.15,−0.05)	
Trend test [b]		<0.001		<0.001		<0.001		<0.001
Every average 5 μg/m^3/ year decrease	0.27 (0.21,0.32)		0.27 (0.21,0.32)		0.26 (0.21,0.32)		0.27 (0.21,0.32)	

Abbreviations: $PM_{2.5}$: particulate matter with an aerodynamic diameter of 2.5 μm or less; FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s; MEF25-75: midexpiratory flow between 25 and 75% of the forced vital capacity; Coef, coefficient; HR, hazard ratio; CI, confidence interval.

[a] Model 1: no adjustment; Model 2: adjusted for age, gender, BMI, and education; Model 3: further adjusted smoking, alcohol drinking, leisure-time physical activity, occupational exposure to dust & organic solvent, and season; Model 4: further adjusted for baseline $PM_{2.5}$ concentration.

[b] The trend test was performed across $\Delta PM_{2.5}$/year tertile with the corresponding tertile treated as a numeric variable (an ordinal variable code as 1–3.

Table 3
The association between $\Delta PM_{2.5}$ and COPD development.

Models [a]	Model 1		Model 2		Model 3		Model 4	
	HR(95% CI)	*P*	HR(95% CI)	*P*	HR(95% CI)	*P*	HR(95% CI)	*P*
1st Tertile (−34.28 ~ −1.05)	0.71 (0.65,0.83)		0.76 (0.69, 0.83)		0.76 (0.69, 0.83)		0.75 (0.68, 0.82)	
2nd Tertile (−1.05 ~ 0.37)	Ref		Ref		Ref		Ref	
3rd Tertile (0.37 ~ 31.46)	0.92 (0.78,1.00)		0.93 (0.84,1.02)		0.93 (0.85,1.02)		0.94 (0.86,1.03)	
Trend test [b]		<0.001		<0.001		<0.001		<0.001
Every average 5 μg/m^3 decrease	0.87 (0.82, 0.92)		0.90 (0.84,0.95)		0.89 (0.84, 0.95)		0.88 (0.83, 0.93)	

Abbreviations: $PM_{2.5}$: particulate matter with an aerodynamic diameter of 2.5 μm or less.

[a] Model 1: no adjustment; Model 2: adjusted for age, gender, BMI, and education; Model 3: further adjusted smoking, alcohol drinking, leisure-time physical activity, occupational exposure to dust & organic solvent, and season; Model 4: further adjusted for baseline $PM_{2.5}$ concentration.

[b] The trend test was performed across $\Delta PM_{2.5}$ tertile with the corresponding tertile treated as a numeric variable (an ordinal variable code as 1–3).

(HR: 0.94; 95 %CI: 0.86, 1.03). On average, every 5 μg/m^3 improvement in $PM_{2.5}$ was associated with a 12% (95 %CI: 7%, 17%) decrease in risk of COPD development.

Subgroup analyses are presented in Tables S2 to S3. They generally yielded similar results. Association of $\Delta PM_{2.5}$/year with annual change of FEV1, MEF25-75, and FEV1/FVC significantly differed between male and female participants. Wherease, only the relationships of $\Delta PM_{2.5}$/year with annual change of FEV1/FVC significantly differed across smoking status. Obesity individual had a slightly larger reduction in risk of COPD compared with those with normal weight. The sensitivity analyses also generally yielded similar results (Tables S4-S6, and S8). However, restricting to participants who did not move during the study period seemed to yield a stronger association with change of $PM_{2.5}$ exposure (Tables S7 and S8).

4. Discussion

This large cohort study demonstrates that improvements in long-term exposure to $PM_{2.5}$ are significantly associated with a better lung function and a decreased risk of COPD development. On average, every 5 μg/m^3/year decrease in $PM_{2.5}$ was associated with a better of 19.93 mL/year, 12.76 mL/year, 70.22 mL/s/year and 0.27%/year in FEV_1,

FVC, MEF25-75 and FEV_1/FVC, respectively. Consistently, 5 μg/m^3 decrease of $PM_{2.5}$ was associated with a 12% reduced risk of incident COPD.

We identified several studies based on the three cohorts [i.e. Swiss study on air pollution and lung disease in adults (SAPALDIA) (Schikowski et al., 2013; Downs et al., 2007; Thun et al., 2014), Study on the influence of Air pollution on Lung function, Inflammation and Aging (SALIA) (Huls et al., 2019) and a cohort from the Netherlands (Boogaard et al., 2013)] that have prospectively investigated the beneficial effects of air quality improvement on lung function in adults. However, the results were inconsistent. The SAPALDIA cohort reported that decreased PM_{10} was associated with an attenuated decrease in lung function parameters of FEV_1, FEV_1/ FVC ratio, and FEF_{25-75} but not with FVC (Schikowski et al., 2013; Downs et al., 2007; Thun et al., 2014). The SALIA cohort investigated several pollutants. They found that a decrease in NO_2/NO_x was associated with attenuated decrease in FEV_1 and FEV_1/ FVC ratio but not in FVC. For particulate matter, their results showed that a decrease in PM_{10} was associated with attenuated decrease in FEV_1/ FVC ratio but not with FEV_1 and FVC, while change in $PM_{2.5}$ had no associations with FEV_1, FVC, or FEV_1/FVC ratio (Huls et al., 2019). The cohort from the Netherlands showed that reductions in the concentrations of soot, NO_2, and NOx but not PM_{10}/$PM_{2.5}$ were associated with attenuated decrease in FVC (Boogaard et al., 2013).

Our study found that air quality improvement has significant beneficial effects on all four parameters (i.e., FEV_1, FVC, MEF25-75 and FEV_1/FVC). However, it might be difficult to compare our results with the aforementioned studies directly because all of them were conducted in European countries, where the air pollution is much lower. Besides, there are differences in population ethnicities, sample sizes and many aspects in research methods (e.g., $PM_{2.5}$ measurement methods and frequency of spirometry tests).

In line with the beneficial effects on lung function, we firstly found that decreased $PM_{2.5}$ is associated with a reduced risk of 12% in COPD development, which corroborates the evidence that improvement in PM exposure was associated with reduced rates of respiratory symptoms (Schindler et al., 2009). However, when the $\Delta PM_{2.5}$ was categorized into tertiles, we did not observe a statistically significant difference between participants in the third and the second tertile (Table 3). The exact reason is unclear. We identified the incident COPD mainly by the repeated spirometry tests rather than the record of mortality and hospital admission. However, the current study is an open (dynamic) cohort. Participants with severe diseases such as COPD might not come back to the firm for health screening as they might go to hospitals for treatment directly. Thus, we speculate that the survival bias due to the dynamic cohort design might result in the non-significant association of $\Delta PM_{2.5}$ with incident CODP. Further study on this is warranted.

In stratified analysis for lung function, our result showed significantly stronger associations of $\Delta PM_{2.5}$/year with FEV1 and FEV1/FVC, while weaker association with ΔMEF25-75 among male participants. Some studies reported that males were more sensitive to air pollution (Doiron et al., 2019), while others suggested greater vulnerability among females (Adam et al., 2015) or non-significant difference between males and females. (Schikowski et al., 2013). We also observed stronger associations of $\Delta PM_{2.5}$/year with annual change of FEV1/FVC among former smokers than among never and current smokers. Previous study have shown that former smokers were more susceptible to lung function decline after exposure to traffic-related air pollution (Franco Suglia et al., 2008). This discrepancy may be attributed to the "healthy smoker" effect for air pollution (Nyberg et al., 2000). Even though former smokers may have quit smoking due to respiratory symptoms and/or health problems, current smokers might be less sensitive to the effects of tobacco smoking and, subsequently less sensitive to air pollution. In addition, the physiological changes in current smokers (e.g., bronchial mucosal thickening) may make them less susceptible to additional pollutants exposure (O'Neill et al., 2003).

In stratified analyses for COPD, we fund that obese participants were more sensitive to the association of $\Delta PM_{2.5}$ with COPD development compared with those with normal BMI, which is in line with the UK Biobank (Doiron et al., 2019), ESCAPE (Adam et al., 2015), and SAPALDIA (Schikowski et al., 2013) studies. The possible mechanism for the effect modification by BMI may be partly due to the reduced the expiratory reserve volume and residual capacity through airway calibre among obese participants (Jones and Nzekwu, 2006).

The associations of change in $PM_{2.5}$ with change in lung function and incident COPD among those participants who did not move during the study seemed to be stronger than those among all participants. This phenomenon was in line with previous studies evaluating the associations between air pollution and non-communicable chronic diseases. (Bakolis et al., 2020; Villeneuve et al., 2002; Bilenko et al., 2015) The stronger associations among non-movers compared with movers suggest that chronic $PM_{2.5}$ exposure is of greater relevance than recent exposure.

This study has several important strengths. First, the longitudinal study design with a relatively long study period (from 2001 to 2014) makes it possible for us to investigate both the adverse effects of air deterioration and the beneficial effects of air improvement on lung function and COPD development. Second, the large sample size not only provides us with sufficient power to detect the small effect of ambient $PM_{2.5}$, but also enabled us to perform a series of stratified and sensitivity analyses to test the robustness of results. Third, all health data were retrieved from a standard health screening program, which can minimize investigator bias. Fourth, we minimized triggering effect on COPD by short-term exposure to $PM_{2.5}$ because we identified the incident COPD using the repeated spirometry tests or self-reported of physician-diagnosed COPD rather than using mortality or hospital admission data. Neither mortality nor hospital admission studies can ambiguously distinguish acute from long-term effects on the development of the underlying pathophysiological changes (Schikowski et al., 2014a). Finally, we used a spatio-temporal model based on high-resolution (1 km^2) satellite data to estimate the $PM_{2.5}$ exposure for each participant's address. This technology allowed us to overcome the space coverage limitations that typically occur when data is only obtained from monitoring stations. It also enables us to identify individual levels of exposure and to track $PM_{2.5}$ air pollution levels over time.

The findings should also be interpreted with some caution. First, we don't have information on gaseous pollutants, such as NOx and ozone. Therefore, we are not sure whether the observed associations were specifically caused by $PM_{2.5}$ or a combination of the pollutants. However, $PM_{2.5}$ pollutant is highly correlated with these gaseous pollutants, suggesting that we should not include them in the model for adjustment. Second, the exposure level of $PM_{2.5}$ was assigned to the participant's fixed address. Information on the patterns of daily activities was not available. More advanced technologies are needed to assess the exposure of personal exposure more accurately in future studies. Third, we did not collect information on the duration of residence for those participants who changed an address in the study. However, the sensitivity analysis excluding these participants yielded similar results (Table S7), suggesting that this limitation did not affect our conclusions. Forth, the incidence of COPD was mainly diagnosed based on the spirometry test during the participants' follow-up visits. The exact onset date of COPD incidence might be difficult to determine because patients might have already developed COPD before the follow-up visit. An alternative approach considering the interval censoring would have been used to correct such bias, if any. (Zhang and Sun, 2010). In addition, $PM_{2.5}$ fluctuations near the date of spirometry test might slightly affect the participants' lung function. More advanced technologies are needed to assess the exposure of personal exposure more accurately in future studies. Finally, we diagnosed COPD based only on pre-spirometry tests, which were similar to ESCAPE five-cohort analysis (Schikowski et al., 2014b) and the UK Biobank study (Doiron et al., 2019). Some participants might have airflow limitation but not clinical COPD. The wrongly classification as having COPD might bias the association However, the misclassification is random because there is no evidence showing that

participants with higher $PM_{2.5}$ exposure were more likely to be misdiagnosed as having COPD. We thus speculated this limitation should not change the direction of our findings. To minimize the bias by this limitation, we excluded participants with a history of asthma or lung cancer at baseline. Furthermore, our findings were consistent when using GLI-2012 reference values for LLN to define COPD.

5. Conclusion

In conclusion, we firstly found that the improvement of ambient $PM_{2.5}$ is associated with better lung function parameters of FEV_1, FVC, MEF25-75, and FEV_1/FVC and a decreased risk of COPD development. On the other hand, deterioration of ambient $PM_{2.5}$ exposure is associated with worse lung function. This finding enhances our understanding on the causal relationship between air pollution and pulmonary health, suggesting air pollution mitigation is one of the effective strategies that can combat the global epidemic of COPD.

Author statement

XQL conceived and designed the study. LYC, CQL, AKHL, TT, and XQL acquired the data. YCB, and CG searched literature. YCB and XQL analysed the data, interpreted the results, and drafted the manuscript. All authors critically revised the manuscript. XQL obtained the funding. LYC, AKHL, TT, and XQL supervised this study.

Declaration of Competing Interest

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

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2021.106706.

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