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Title: Chronic effects of ambient air pollution on lung function among Chinese children

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ABSTRACT

Objectives: To examine the association between long-term exposure to air pollution and lung function among Chinese schoolchildren in Southern China.

Methods: We conducted a cross-sectional study among 3,168 schoolchildren (aged 8-10 years) in three districts of Hong Kong. Annual means of ambient PM_{10}, SO_2, NO_2 and O_3 from 1996 to 2003 were used to estimate individual exposure of the subjects. Children's lung function was measured for FVC, FEV_1, FEF_{25-75} and FEF_{75}. Analysis of covariance was performed separately by gender to estimate the impact of air pollution on lung function, with adjustment for socioeconomic characteristics, respiratory morbidities, height and weight, physical activity, indoor air contaminants, and short-term exposure to the air pollutants.

Results: After controlling for potential confounding factors, FEV_1, FEF_{25-75} and FEF_{75} for boys in high-pollution district were significantly lower than those in low-pollution district by 3.0%, 7.6% and 8.4% respectively. No significant differences were found for girls. Results from the comparison between moderate- and high-pollution districts were similar. There were no differences between children in low- and moderate-pollution districts except that a higher FEF_{75} was found in boys in MPD. PM_{10} is the strong pollutant responsible to the lung function deficit. Asthmatic children were more vulnerable to exposure to air pollution.

Conclusions: Long-term exposure to higher ambient air pollution levels was associated with lower lung function in Chinese schoolchildren, especially among boys. Adverse effects were observed on both large and small airways, with a stronger effect on the latter.

BACKGROUND

Lung function is known as an objective measure of respiratory health and an early predictor of cardiorespiratory morbidity and mortality. Acute effects of ambient air pollution on lung function has been well documented in animal models and human chamber studies, as well as epidemiological studies such as panel studies and pollution episodes.[1-3] However, chronic effects at current ambient concentrations are still not clear.[1] Children are a particularly vulnerable population because they spend more time outdoors, are more physically active, and have higher ventilation rates than adults. Furthermore, children's lung is growing and their immunization system is still immature.[4]

An increasing number of studies has been focused on the long-term effects of ambient air pollution on children's lung function. However, the outcomes are equivocal.[5-11] Baseline findings from the Children's Health Study (CHS) in the USA showed several air pollutants (including PM_{10}, $PM_{2.5}$, acid vapor, NO_2 and O_3) were associated with lung function, with girls and those who spent more time outdoors being more vulnerable than their counterparts.[5] After an 8-year follow-up, the study revealed the strongest associations between FEV_1 and a correlated set of pollutants, specifically, acid vapor, $PM_{2.5}$ and elemental carbon and similar effects in boys and girls.[6-8] However, no association with O_3 was found in the study period. A 3.5-year Austrian cohort study on O_3 concluded that medium-term effects (exposure for several months) on lung growth in school children were evident, whilst long-term effects were not associated with lung function partially due to reversibility.[11] Most studies were conducted in Western countries and evidence in China is scarce, though it has the largest population and the third largest land area in the world.[12-14] Owing to differences in ethnicity and lifestyle of children between China and western countries, it might not be appropriate to directly use results from overseas studies for Chinese children. In this cross-sectional study, we examined the relationship between long-term exposure to ambient air pollution and lung function among Chinese children. We studied subjects exposed to three levels of air pollution in order to test whether there would be a monotonic exposure-response relationship between air pollution and lung function. We also explored gender differences in the children's response to air pollution and adverse effects among asthmatic children.

METHODS

Selection of districts and participants

The study was conducted from March to June of 2004. Three districts, designated as low, moderate and high pollution districts, were selected based on historical data on annual mean concentrations of

PM_{10}, as it is the major pollutant in Hong Kong and existing evidence suggests that particulate matter may be the most relevant air pollutant to cause children's lung function deficit by long-term exposure.[6-8 14] Three to four primary schools in each district, which are located within 1 km from the local air monitoring station, were invited to participate into the study. The selected schools were all public schools and similar in school size, number of students, source of students, area of playgrounds, and sports facilities in order to minimise differences across schools. All eligible students in grades three and four were investigated and written consents were obtained from their parents in advance. Approval was obtained from the Ethics Committees at the Chinese University of Hong Kong. The following are the selection criteria of our subjects: 1) Children who had been currently living in their school district for more than 12 consecutive months before the study; 2) Children of Chinese ethnicity; 3) Children aged 8-10 years.

Data collection

Ambient air pollutants were studied for PM_{10}, NO_2, SO_2 and O_3, which were continuously measured in Hong Kong.[14] Annual mean average in 1996-2003 and in the year prior to the study (May 2003 to April 2004) were used to estimate the life-time and current exposure levels of the participants respectively. Two measures of short-term exposure were also collected: one was the hourly mean average in the period of 7am to 2pm on the 13 test days; and the other was the 24-hour means for PM_{10}, NO_2, SO_2 and 8-hour maximal mean for O_3 on one day before the test. Daily mean temperature (°C) and daily mean relative humidity (%) on the test days were also retrieved as potential confounding factors.

Two self-administered questionnaires were developed based on the Children's Questionnaire of the American Thoracic Society (ATS-DLD-78-C) to collect the children's personal and household information.[15] Parents reported on socioeconomic status, children's current and past history of respiratory conditions, parental history of asthma, housing indoor environmental factors, as well as the children's birth weight, birth place and history of breastfeeding. Students reported on their gender, smoking habits, time spent outdoors, amount and type of physical activities, participation in sports teams in their schools and playing with furry toys in the past 12 months. Height (cm) and weight (kg) were measured following standard anthropometric methods. Body mass index (BMI, kg/m^2) was calculated.

Forced expiratory spirogram and maximal expiratory flow-volume curve were simultaneously measured on four Vitalograph® Compact Dry Spirometers according to recommendations and cautions by the American Thoracic Society.[16] Each student was measured five times with correct standing posture and at least three acceptable tests were obtained.[16] Forced vital capacity (FVC), one-second forced expiratory volume (FEV_1), forced expiratory flow between the 25th and 75th of FVC (FEF_{25-75}), and forced expiratory flow at 75% of FVC (FEF_{75}) were derived from the best curve of each student. The volumes were directly read from charts at body temperature and pressure, saturated with water vapour (BTPS) condition, on the presumption that the temperature was 23±2°C. Predicted FVC, FEV_1 and FEF_{25-75} (%) were calculated from the children's height (cm) separately by gender according to reference values for Chinese children.[17] R^2 of the equations ranged from 0.45 to 0.90. R^2 values for boys were higher than for girls, with FVC being the highest and FEF_{25-75} being the lowest.

Data analysis

Data analysis was performed using the SPSS for windows 16.0 version. One way analysis of variance (ANOVA) and analysis of covariance (ANCOVA) was performed to compare children's lung function among the three districts with different air pollution levels before and after adjustment for potential confounders. Least significant difference was applied for pair-wise comparisons. Adjusted mean and mean difference and their standard error (SE) were derived. Background variables, including gender (for asthmatic children only), age, father's job and birth place, were adjusted for regardless of their significance. Other confounders were selected in a stepwise manner by multiple linear regression model using $P<0.10$ and $P<0.15$ as entry and removal criteria with adjustment for the background variables. Linearity was tested with scatterplots for each pair of dependant and independent variables. Suitable variable transformation would be performed where there was a need. Multicollinearity among independent variables, as well as normality, linearity, homoscedasticity, and independence of residuals were tested for assumptions of the linear regression models when building up the models. Tolerance was checked for multicollinearity and residuals plots were plotted for checking the other assumptions. Appropriate nonlinear transformation would be made where necessary. The two measures of short-term air pollutant concentrations (on and one day before the test) were separately selected for each outcome.

RESULTS

Figure 1 depicts the long-term trends of pollutants in the three districts. Annual mean averages in 1996-2003 and annual means in the past year were also presented. Short-term pollutant concentrations varied from 20-94 μg/m^3 for PM_{10}, 25–97 μg/m^3 for NO_2, 8–82 μg/m^3 for SO_2 and 6–109 μg/m^3 for O_3. Ranges of air temperature and relative humidity were 19.7– 5.1°C and 72–87% respectively.

Of 3,186 eligible students in 11 primary schools, 82.9% (n=2,641) took part in the study. Around 90% of the participants (n=2,391) completed both the questionnaire survey and lung function test. There were 331 participants with data excluded due to failure to meet our selection criteria. Finally 2,060 children were included in data analysis, consisting of 1,064 boys and 996 girls. Table 1 compares the distribution of their personal and household characteristics and Table 2 compares Children's age, anthropometry and lung function. Boys had significant higher values for all lung function indices than girls except for FEF_{75}. The between-group differences by district achieved significance in FEV_1, FEF_{25-75} and FEF_{75} among boys, with the highest means being found in MPD. The measured lung function was lower than their predicted values except for FVC in boys, with measured FEF_{25-75} being only 64.4-75.8% of predicted FEF_{25-75} in both genders. The between-group differences achieved statistical significance in predicted FEF_{25-75} in boys, as well as predicted FVC and predicted FEV_1 in girls.

Table 1 Characteristics of the subjects

	Boys (n=1064)			Girls (n=996)		
	LPD (n=457)	MPD (n=365)	HPD (n=245)	LPD (n=403)	MPD (n=329)	HPD (n=264)
Personal characteristics						
Blue-collar job of father [a] (%)	61.4***	84.5***	79.8***	54.9***	80.6***	81.3***
Born in Hong Kong (%)	92.4***	77.6***	86.7***	93.7***	75.3***	86.0***
Low birth weight [b] (%)	10.1	8.1	7.6	9.3	13.2	9.4
Having been breastfed (%)	27.8***	47.5***	26.6***	27.8**	36.2**	17.6**
Parental asthma (%)	4.5	2.5	5.7	5.4	4.8	7.2
Wheezing (%)	5.0	4.8	5.9	3.6	4.8	6.0
Cough (%)	19.7	24.9	18.9	16.2***	26.3***	27.2***
Phlegm (%)	34.0	31.3	33.8	31.0	32.7	38.0
Current asthma (%)	3.1	2.6	4.2	2.1	1.7	2.5
Life-time asthma (%)	7.4	7.2	8.8	6.6	5.9	7.2
Current bronchitis (%)	12.8	9.7	13.0	10.1	10.5	11.5
Life-time bronchitis (%)	50.7	48.1	48.7	49.8	50.3	51.8
Active smoking (%)	0.2	1.3	0.8	0.0	0.0	0.0
Being physically active [c] (%)	41.9***	29.3***	38.8***	39.3**	29.8**	30.6**
Participated in sports team (%)	26.4***	13.7***	25.1***	23.6*	17.2*	23.0*
More outdoors [d] (%)	50.7	48.1	48.7	49.8	50.3	51.8
Housing environmental characteristics						
Mould in the home (%)	24.3***	21.1***	12.9***	22.9#	22.2#	16.5#
Having new furniture (%)	15.9	18.6	16.3	18.7	21.9	18.3
Incense burning (%)	20.8*	29.0*	24.3*	17.5	20.5	20.9
Passive smoking (%)	16.5***	29.5***	24.0***	17.8***	35.1***	30.9***

LPD: low-pollution district; MPD: moderate-pollution district; HPD: high-pollution district.
Chi-square test was used; #: $P<0.10$; *: $P<0.05$; **: $P<0.01$; ***: $P<0.001$.
a Including service workers, shop sales workers, skilled workers, unskilled workers, and other kindred workers.
b Birth weight less than 2500 g.
c Taking part in sports and/or vigorous free play at least three times a week for at least 30 minutes each time.
d Indicating that children who spent more hours per week outdoors than the median value for their respective district and gender.

Table 2 Distribution of age, anthropometry and lung function of the participants by gender

	All students	LPD	MPD	HPD
	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)
Boys				
Age *(year)*	9.00 *(0.70)*	8.98 *(0.71)*	9.05 *(0.71)*	8.96 *(0.66)*
Height *(cm)*	134.6 *(6.8)*	134.3[#] *(6.8)*	135.3[#] *(6.8)*	134.2[#] *(6.5)*
Weight *(kg)*	32.4 *(8.1)*	32.1 *(8.3)*	32.8 *(8.3)*	32.1 *(7.4)*
BMI *(kg/m^2)*	17.7 *(3.2)*	17.6 *(3.2)*	17.7 *(3.3)*	17.7 *(3.1)*
FVC *(L)*	1.830 *(0.344)*	1.813[#] *(0.334)*	1.861[#] *(0.352)*	1.813[#] *(0.348)*
FEV_1 *(L)*	1.598 *(0.310)*	1.589[*] *(0.301)*	1.631[*] *(0.311)*	1.565[*] *(0.320)*
FEF_{25-75} *(L/s)*	1.814 *(0.523)*	1.803[***] *(0.514)*	1.896[***] *(0.511)*	1.711[***] *(0.540)*
FEF_{75} *(L/s)*	0.880 *(0.342)*	0.858[***] *(0.333)*	0.963[***] *(0.341)*	0.797[***] *(0.335)*
Predicted FVC *(%)*[a]	101.2 *(15.4)*	100.9 *(14.6)*	101.1 *(15.7)*	101.6 *(16.5)*
Predicted FEV_1 *(%)*[a]	98.6 *(16.0)*	98.8 *(15.1)*	99.1 *(16.4)*	97.7 *(17.1)*
Predicted FEF_{25-75} *(%)*[a]	73.3 *(20.1)*	73.3[**] *(19.5)*	75.8[**] *(19.8)*	69.7[**] *(21.1)*
Girls				
Age *(year)*	8.95 *(0.71)*	8.96 *(0.72)*	8.96 *(0.71)*	8.94 *(0.69)*
Height *(cm)*	134.4 *(7.4)*	134.1 *(7.2)*	135.1 *(7.3)*	133.9 *(7.8)*
Weight *(kg)*	31.0 *(7.6)*	30.7 *(7.0)*	31.2 *(7.7)*	31.1 *(8.1)*
BMI *(kg/m^2)*	17.0 *(2.9)*	16.9 *(2.8)*	16.9 *(2.9)*	17.2 *(3.1)*
FVC *(L)*	1.684 *(0.332)*	1.679 *(0.316)*	1.678 *(0.335)*	1.697 *(0.352)*
FEV_1 *(L)*	1.479 *(0.307)*	1.485 *(0.290)*	1.476 *(0.305)*	1.474 *(0.333)*
FEF_{25-75} *(L/s)*	1.727 *(0.528)*	1.758[#] *(0.508)*	1.738[#] *(0.527)*	1.667[#] *(0.554)*
FEF_{75} *(L/s)*	0.860 *(0.357)*	0.844[#] *(0.317)*	0.899[#] *(0.336)*	0.836[#] *(0.429)*
Predicted FVC *(%)*[a]	97.9 *(14.6)*	98.4[*] *(14.5)*	96.0[*] *(14.5)*	99.6[*] *(14.6)*
Predicted FEV_1 *(%)*[a]	93.7 *(15.3)*	94.7[*] *(14.9)*	92.0[*] *(15.3)*	94.5[*] *(15.8)*
Predicted FEF_{25-75} *(%)*[a]	66.1 *(18.5)*	67.6[#] *(17.8)*	65.8[#] *(19.0)*	64.4[#] *(18.8)*

LPD: low-pollution district; MPD: moderate-pollution district; HPD: high-pollution district. One-way ANOVA was used. SD: standard deviation.
#: $P<0.10$; *: $P<0.05$; **: $P<0.01$; ***: $P<0.001$.
a: predicted FVC, FEV_1 and FEF_{25-75} were calculated with lung function reference values for Chinese Children.[17]

Table 3 Adjusted means (M) and mean differences (MD) for lung function by gender

	LPD M *(SE)*	MPD M *(SE)*	HPD M *(SE)*	MPD-LPD M *(SE)*	HPD-LPD M *(SE)*	HPD-MPD M *(SE)*	Adjusted R^2	Covariates adjusted
Boys								
FVC *(L)*	1.839 *(0.016)*	1.848 *(0.017)*	1.819 *(0.021)*	0.009 *(0.020)*	-0.020 *(0.023)*	-0.029 *(0.023)*	0.41	age (+)$^{\#}$, blue-collar job of father, born in Hong Kong, height (+)***, weight (+)***, SO_2 on previous day (-)**
FEV_1 *(L)*	1.613* *(0.015)*	1.623* *(0.016)*	1.566* *(0.020)*	0.009 *(0.018)*	-0.048* *(0.021)*	-0.057** *(0.022)*	0.36	age, blue-collar job of father, born in Hong Kong, height (+)***, BMI (+)**, SO_2 on previous day (-)***
FEF_{25-75} *(L/s)*	1.743*** *(0.045)*	1.805*** *(0.047)*	1.610*** *(0.051)*	0.062 *(0.037)*	-0.133** *(0.043)*	-0.195*** *(0.043)*	0.13	age (+)*, blue-collar job of father, born in Hong Kong, height (+)***, wheezing (-)*, SO_2 on previous day (-)***
FEF_{75} *(L/s)*	0.806*** *(0.034)*	0.878*** *(0.034)*	0.738*** *(0.038)*	0.072** *(0.027)*	-0.068$^{\#}$ *(0.035)*	-0.140*** *(0.035)*	0.15	age, blue-collar job of father, born in Hong Kong, height (+)***, wheezing (-)*, life-time bronchitis (-)*, SO_2 on previous day (-)$^{\#}$
Girls								
FVC *(L)*	1.699 *(0.018)*	1.681 *(0.018)*	1.709 *(0.021)*	-0.017 *(0.019)*	0.011 *(0.021)*	0.028 *(0.021)*	0.49	age (+)**, blue-collar job of father$^{\#}$, born in Hong Kong, height (+)***, weight (+)***, participated in sports team (+)***, incense burning (-)**, SO_2 on previous day (-)*
FEV_1 *(L)*	1.498 *(0.018)*	1.473 *(0.018)*	1.478 *(0.021)*	-0.025 *(0.019)*	-0.020 *(0.020)*	0.005 *(0.021)*	0.39	age (+)**, blue-collar job of father, born in Hong Kong, height (+)***, weight (+)***, participated in sports team (+)**, incense burning (-)*, passive smoking (-)*, SO_2 on previous day (-)*
FEF_{25-75} *(L/s)*	1.596 *(0.060)*	1.569 *(0.060)*	1.566 *(0.064)*	-0.026 *(0.041)*	-0.029 *(0.050)*	-0.003 *(0.047)*	0.16	age (+)**, blue-collar job of father, born in Hong Kong, height (+)***, wheezing (-)*, parental asthma (-)**, participated in sports team (+)*, incense burning (-)$^{\#}$
FEF_{75} *(L/s)*	0.712 *(0.050)*	0.741 *(0.051)*	0.709 *(0.051)*	0.029 *(0.026)*	-0.002 *(0.027)*	-0.031 *(0.028)*	0.14	age (+)$^{\#}$, blue-collar job of father, born in Hong Kong, height (+)***, current asthma (-)*, parental asthma (-)*, participated in sports team (+)$^{\#}$, being physically active (+)*

LPD: low-pollution district; MPD: moderate-pollution district; HPD: high-pollution district.
SE: standard error.
#: P<0.10; *: P<0.05; **: P<0.01; ***: P<0.001.
(+): positive relationship; (-): negative relationship.

Table 3 presents the adjusted means and mean differences in lung function after controlling for confounders. Lung function among boys in HPD were significantly lower than those in LPD and MPD by 0.048 L (3.0%) and 0.057 L (3.5%) for FEV_1, 0.133 L/s (7.6%) and 0.195 L/s (10.8%) for FEF_{25-75}, and 0.068 L/s (8.4%) and 0.140 L/s (15.9%) for FEF_{75}. Differences between LPD and MPD were insignificant except that a higher FEF_{75} was observed among boys in MPD (by 0.072 L/s or 8.9%). Girls appeared to be less influenced by air pollution exposure compared to boys and no significant differences were found among the districts. Giving PM_{10} is the major pollutant locally, we further estimated lung function changes per unit increase of the annual means for PM_{10} in the three districts. PM_{10} annual means of LPD, MPD and HPD were 48.9, 55.0 and 57.6 μg/m^3 respectively (Figure 1). FEV_1, FEF_{25-75}, and FEF_{75} of boys significantly decreased by 0.008 L, 0.027 L/s, and 0.022 L/s respectively along with a 1 μg/m^3 increase of annual mean for PM_{10} (Table 4). No significant relationship was observed for boy's FVC or for all lung function indicators of girls. The results were in line with those in Table 3.

Table 4 Lung function changes per unit increase of annual means for PM_{10} (1 μg/m^3) in the study districts

	Boys			Girls		
	Change	*(95% CI)*	P value	Change	*(95% CI)*	P value
FVC *(L)*	-0.005	*(-0.012,0.002)*	0.182	0.003	*(-0.003,0.010)*	0.316
FEV_1 *(L)*	-0.008*	*(-0.015,-0.002)*	0.014	-0.001	*(-0.007,0.005)*	0.811
FEF_{25-75} *(L/s)*	-0.027***	*(-0.040, -0.013)*	<0.001	-0.005	*(-0.018,0.008)*	0.491
FEF_{75} *(L/s)*	-0.022***	*(-0.030, -0.013)*	<0.001	-0.00003	*(-0.008,0.008)*	0.993

#: P<0.10; *: P<0.05; **: P<0.01; ***: P<0.001.
Covariates adjusted were the same as those in Table 3.

In the past year before the study, PM_{10} levels in MPD were similar to that in LPD. We therefore combined data from LPD and MPD and compared them to that in HPD to estimate the PM_{10} effects on lung function. The results were similar to our original 3-district analyses. Significant deficits in FEV_1, FEF_{25-75} and FEF_{75} among boys remained but the differences were smaller (decreased by 3.2%, 9.1% and 12.3% respectively). We also compared results of combined data from MPD and HPD with that in LPD to test the NO_2 effects, as the annual mean concentrations in MPD and HPD were similar in the past year. However, no significant relationship was observed.

We compared each lung function index with adjustment for all the same covariates. The results did not change much from the original ones except for a marginally lower FEF_{25-75} among girls in HPD compared to those in LPD (Table 6 of supplementary data). In addition, we compared predicted

FVC, FEV_1 and FEF_{25-75} by district. The results were also similar (Table 7 of supplementary data). Overall, the results across different analyses were similar, suggesting that our findings are robust.

Table 5 examines the relationship between air pollution exposure and lung function among asthmatic children. Asthma prevalence in LPD, MPD and HPD was 2.6%, 2.1% and 3.3% respectively and there was no significant difference across districts without or with adjustment for other confounders (data not shown). Clear exposure-response relationships were observed between air pollution level and all lung function indices among asthmatic children. Adverse effects were higher for flow measures than volume measures and were larger when comparing HPD to LPD than to MPD, with a deficit ranging from 12.2% to 58.2%. The associations observed among non-asthmatic children were similar to those among all students in terms of both direction and magnitude (data not shown).

Table 5 Adjusted means/mean differences (M/MD) for lung function among asthmatic children

	LPD (n=24) M *(SE)*	MPD (n=16) M *(SE)*	HPD (n=18) M *(SE)*	MPD-LPD M *(SE)*	HPD-LPD M *(SE)*	HPD-MPD M *(SE)*	Adjusted R^2	Covariates adjusted
FVC *(L)*	1.726* *(0.079)*	1.652* *(0.104)*	1.515* *(0.093)*	-0.074 *(0.097)*	-0.210* *(0.081)*	-0.137 *(0.095)*	0.57	girl (-)***, age, blue-collar job of father (+)*, born in Hong Kong, height (+)**, BMI (+)*, having been breastfed (+)**, current bronchitis (-)#, having new furniture (-)#
FEV_1 *(L)*	1.518* *(0.083)*	1.481* *(0.092)*	1.264* *(0.095)*	-0.038 *(0.102)*	-0.255** *(0.091)*	-0.217* *(0.102)*	0.48	girl (-)***, age, blue-collar job of father, born in Hong Kong, height (+)***, weight (+)#, having been breastfed (+)**
FEF_{25-75} *(L/s)*	1.582** *(0.152)*	1.384** *(0.164)*	0.860** *(0.185)*	-0.198 *(0.185)*	-0.722*** *(0.189)*	-0.524* *(0.201)*	0.37	girl (-)**, age, blue-collar job of father, born in Hong Kong, height (+)**, having been breastfed (+)#, SO_2 on previous day (-)#
FEF_{75} *(L/s)*	0.735*** *(0.085)*	0.602*** *(0.092)*	0.307*** *(0.103)*	-0.133 *(0.103)*	-0.428*** *(0.105)*	-0.295* *(0.112)*	0.42	girl (-)#, age, blue-collar job of father, born in Hong Kong, height (+)*, having been breastfed (+)#, being physically active (-)#, SO_2 on previous day (-)#

LPD: low-pollution district; MPD: moderate-pollution district; HPD: high-pollution district.
SE: standard error.
#: P<0.10; *: P<0.05; **: P<0.01; ***: P<0.001.
(+): positive relationship; (-): negative relationship.

DISCUSSION

This study revealed that male primary schoolchildren in HPD had significantly reduced lung function, as measured by FEV_1, FEF_{25-75}, and FEF_{75}, when compared to those in LPD and MPD, whilst the adverse effects among girls were not significant. Lung function deficits were larger for the flow measures than the volume measures and among currently asthmatic children.

Our findings support the hypothesis of adverse effects of air pollution on lung function among Chinese schoolchildren, and agree with earlier studies in Southern China.[12 13] Yu et al in a cross-sectional study in Hong Kong indicated that FEV_1 and FEF_{25-75} were significantly lower among boys in a more polluted district compared to those in a less polluted district.[12] Decrements in FEV_1 and FEF_{25-75} were 3.0% and 7.1% respectively, which are of similar magnitude with our findings between HPD and LPD. In that study, similar adverse effects were also observed among girls. A study in Guangzhou followed primary schoolchildren up for six months and revealed significant growth deficits in FEV_1, FEF_{25-75} and FEF_{75} for boys in more polluted areas but not for girls, which is consistent with our findings and suggests that boys are more likely to be adversely affected by exposure to ambient air pollution.[13] In brief, studies from Southern China including this one are generally agreement with most published oversea studies in support of our research hypothesis on outdoor air pollution and children's lung function.[5-7 18-24] However, some studies failed to observe the negative associations.[9 25]

Lung function test has been widely used in clinical practice and epidemiological studies. During the test, lung volumes below about two-thirds of maximal expiration are mainly limited by the physical factors of lower airways and lung parenchyma. The expiratory flows are typically limited by the progression of airway obstruction. Flow limitation in large airways would reduce expiratory flow rates at all lung volumes, whilst flow limitation in small airways would reduce flow rates at low lung volumes.[26] FVC indicates the maximum volume of air exhaled from the lungs in a forced breath, FEV_1 mainly reflects the mechanical properties of large airway, while FEF_{25-75} and FEF_{75} are measures more indicative of peripheral small airway functions.[27] It has been suggested that small airways might receive the highest tissue doses of air pollution and undergo preclinical structural changes before the larger airways are affected.[1] Our finding of larger deficits in FEF_{25-75} and FEF_{75} lent support to this hypothesis along with previous studies.[12 13 21 22 24] In addition, the reduction in FEV_1 also suggests the adverse effect of air pollution exposure on the development of large airways.

As in most observational studies on air pollution and health, it is difficult to distinguish the effects of individual pollutants on lung function as we had three exposure clusters only. The adverse effects observed among boys in HPD were probably contributed by all four pollutants. Our analyses after combining the districts with similar PM_{10} and NO_2 levels respectively revealed significant deficits in FEV_1, FEF_{25-75} and FEF_{75} among boys living in the high-PM_{10} district (HPD) compared to those in the low-PM_{10} districts (combination of MPD and LPD), but no relationship with NO_2. In addition, there was a monotonic exposure-response relationship between PM_{10} and lung function among the asthmatic children, who are more vulnerable than general children (Table 5). The results collectively support our hypothesis that PM_{10} is the most relevant pollutant that impacts on lung function. However, we failed to observe a monotonic relationship between PM_{10} concentration level and lung function. It is MPD not LPD that had the highest lung function of boys, though the differences between the two districts did not reach statistical significance (Table 3). It is possible that the higher O_3 concentrations in LPD may also have adverse effects on lung function, especially on the small airways as reflected by Table 3, and therefore attenuate the favourable effects of low PM_{10} exposure level. In addition, PM_{10} annual means in MPD were even higher than HPD in the beginning two years of the study, but decreased against the time and at last became similarly low with LPD. Our observation suggests that the relatively higher exposure to PM_{10} in the early years may have had not much impact on the children's current lung function or the impact, if existed, may have been caught up with later on when the exposure level lowered down, as observed in previous studies. [1]

We observed gender differences in the adverse effects of air pollution on lung function, with boys being more vulnerable to exposure. In this study, boys were exposed to outdoor air pollution for a longer time than girls. The average mean time spent outdoors in boys was 0.9 hours/week higher than in girls (13.7 hours/week vs. 12.8 hours/week, P=0.011). A higher proportion of boys were physically active (39.2% vs. 34.8%, P=0.047), which could result in the exposure to higher doses of air pollutants by boys than girls. It is reasonable to assume that spending more time outdoors and being more physically collectively contribute to our observation of a strong link between air pollution and lung function in boys. Consistent with our findings, He et al reported a similar pattern.[13] An 8-year cohort study in the USA also observed a large freeway effect in boys than in girls.[23] By contrary, some studies found girls more vulnerable.[5] There were also other studies showing no gender difference.[8] Thus, the gender effects as a modifier on the association between air pollution and lung function are still not clear.

In this study, several potential confounding factors related to lung function or exposure level were studied. We did not find significant influences of socioeconomic status on lung function. Low birth weight and having been breastfed could not explain our outcomes except breastfeeding appeared to have a favorable effect on lung function among asthmatic children. Wheezing, asthma and life-time bronchitis were negatively associated with some lung function indices, while being physically active appears to benefit the lung function in girls only. Several household environmental factors were also examined. Burning incense and passive smoking at home had adverse effects in girls but not in boys, suggesting that girls were more exposed to indoor air pollution. Short-term exposure to ambient air pollution could play a role in the adverse effects on lung function. We found that the 24-hour mean concentration of SO_2 on the day prior to the test was significantly associated with most lung function indices for both sexes.

The followings are limitations of our study. First, we could not establish the temporal order of cause and effect could not be established because of the cross-sectional study design. Moreover, ambient air pollutant concentrations were used as a proxy of individual exposure, which would result in exposure misclassification. Although lung function test has been widely used in epidemiological studies, it is highly dependent on the subjective efforts of the subjects. Several attempts were made during the test to minimise potential measurement bias. All tests were performed in the morning time at school to avoid circadian variation. Each spirometer was operated by the same trained investigator throughout the whole study and calibration was undertaken before and after each test day. In addition, all students were briefed in detail and had observed demonstrations before being tested. They were also asked to keep the standard body and head position and received verbal encouragements during the test. The lack of post-bronchodilator lung function is a limitation as it would provide more information regarding whether the pollution related effect on lung function was reversible or not.[28 29] In our future studies, we would include this important measure such that we can assess the possible reversibility of lung function impairment.

In conclusion, we found that long-term exposure to higher ambient air pollution levels was associated with lower lung function in Chinese schoolchildren, especially among boys. Adverse effects were observed on both large and small airways, with a stronger effect on the latter. This inverse relationship was independent of short-term exposure to air pollution. Our study provides evidence to support stricter air pollution control measures in Hong Kong and China to protect lung of the children. A cohort study with a long follow-up period would provide better insight on the effect of air pollution on the rate of lung growth in children, and on the gender-different response to exposure.

Contributorship

Dr. Gao designed the study, conducted the survey, did the data analysis and wrote up the MS. Prof. Chan participated in writing up the MS and revised it. Prof. Li and Prof. He revised the MS. Prof. Wong led and supervised the study and revised the MS.

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Competing interests

None

Funding

None

What is known about this topic

- Exposure to ambient air pollution can cause diverse adverse health effects.
- Chronic effects on children’s lung function and lung growth are still not very clear.
- Studies in China are scarce though it has the largest population and second largest land area in the world.

What this paper adds

- Our findings add to the evidence of the chronic adverse effects on large and small airways in Chinese boys, but not in girls.
- The observed effects are independent of short-term exposure.
- Our findings suggest that there is a need of stricter air pollution control measures in China to protect lung of the children.

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Table 6 Adjusted means (M) and mean differences (MD) for measured lung function by gender after adjustment for the same covariates

	LPD	MPD	HPD	MPD-LPD	HPD-LPD	HPD-MPD	Adjusted R^2
	M *(SE)*	M *(SE)*	M *(SE)*	M *(SE)*	M *(SE)*	M *(SE)*	
Boys							
FVC *(L)*	1.879	1.878	1.852	0.000	-0.027	-0.027	0.390
	(0.036)	*(0.037)*	*(0.038)*	*(0.021)*	*(0.024)*	*(0.025)*	
FEV_1 *(L)*	1.628*	1.631*	1.576*	0.003	-0.052*	-0.055*	0.345
	(0.033)	*(0.034)*	*(0.035)*	*(0.020)*	*(0.022)*	*(0.023)*	
FEF_{25-75} *(L/s)*	1.715***	1.780***	1.569***	0.065	-0.145***	-0.211***	0.141
	(0.064)	*(0.067)*	*(0.068)*	*(0.038)*	*(0.043)*	*(0.044)*	
FEF_{75} *(L/s)*	0.815***	0.895***	0.726***	0.080**	-0.090**	-0.169***	0.161
	(0.042)	*(0.043)*	*(0.044)*	*(0.025)*	*(0.028)*	*(0.029)*	
Girls							
FVC *(L)*	1.652	1.643	1.658	-0.009	0.005	0.015	0.493
	(0.037)	*(0.038)*	*(0.039)*	*(0.020)*	*(0.021)*	*(0.022)*	
FEV_1 *(L)*	1.420	1.397	1.404	-0.023	-0.016	0.007	0.417
	(0.036)	*(0.037)*	*(0.038)*	*(0.019)*	*(0.021)*	*(0.021)*	
FEF_{25-75} *(L/s)*	1.536#	1.503#	1.439#	-0.034	-0.098*	-0.064	0.171
	(0.075)	*(0.076)*	*(0.077)*	*(0.040)*	*(0.043)*	*(0.044)*	
FEF_{75} *(L/s)*	0.679	0.723	0.679	0.044	-0.001	-0.045	0.171
	(0.051)	*(0.052)*	*(0.053)*	*(0.028)*	*(0.030)*	*(0.030)*	

LPD: low-pollution district; MPD: moderate-pollution district; HPD: high-pollution district.

SE: standard error.

#: P<0.10; *: P<0.05; **: P<0.01; ***: P<0.001.

Covariates adjusted: age, blue-collar job of father, born in Hong Kong, height, weight, BMI, wheezing, current asthma, life-time bronchitis, parental asthma, participated in sports team, being physically active, incense burning, passive smoking, and SO_2 on previous day.

Table 7 Adjusted means (M) and mean differences (MD) for predicted lung function by gender

	LPD	MPD	HPD	MPD-LPD	HPD-LPD	HPD-MPD	Adjusted R^2	Covariates adjusted
	M *(SE)*	M *(SE)*	M *(SE)*	M *(SE)*	M *(SE)*	M *(SE)*		
Boys								
Predicted FVC *(%)*	101.56 *(0.95)*	101.54 *(1.00)*	100.80 *(1.24)*	-0.02 *(1.15)*	-0.76 *(1.33)*	-0.74 *(1.35)*	0.010	age, blue-collar job of father, born in Hong Kong, weight (-)#, SO_2 on previous day (-)***
Predicted FEV_1 *(%)*	99.50# *(0.98)*	99.68# *(1.03)*	96.73# *(1.28)*	0.18 *(1.19)*	-2.78* *(1.37)*	-2.95* *(1.39)*	0.014	age (-)#, blue-collar job of father, born in Hong Kong, BMI, SO_2 on previous day (-)***
Predicted FEF_{25-75} *(%)*	70.72*** *(1.86)*	72.99*** *(1.92)*	65.32*** *(2.08)*	2.27 *(1.51)*	-5.40** *(1.74)*	-7.67*** *(1.77)*	0.026	age, blue-collar job of father, born in Hong Kong, wheezing (-)*, SO_2 on previous day (-)***
Girls								
Predicted FVC *(%)*	98.36 *(1.08)*	96.91 *(1.11)*	99.20 *(1.26)*	-1.45 *(1.19)*	0.84 *(1.26)*	2.29 *(1.29)*	0.028	age, blue-collar job of father, born in Hong Kong, weight, participated in sports team (+)**, incense burning (-)*, SO_2 on previous day (-)*
Predicted FEV_1 *(%)*	94.88 *(1.19)*	92.98 *(1.18)*	94.30 *(1.35)*	-1.90 *(1.22)*	-0.58 *(1.32)*	1.32 *(1.33)*	0.032	age, blue-collar job of father, born in Hong Kong, weight (-)*, participated in sports team (+)***, incense burning (-)*, passive smoking, SO_2 on previous day (-)*
Predicted FEF_{25-75} *(%)*	61.40 *(2.26)*	59.84 *(2.29)*	58.40 *(2.33)*	-1.56 *(1.52)*	-3.00 *(1.56)*	-1.44 *(1.62)*	0.032	age (+)*, blue-collar job of father, born in Hong Kong, wheezing (-)**, parental asthma (-)*, participated in sports team (+)**, incense burning

LPD: low-pollution district; MPD: moderate-pollution district; HPD: high-pollution district.

SE: standard error.

#: P<0.10; *: P<0.05; **: P<0.01; ***: P<0.001.

(+): positive relationship; (-): negative relationship.