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Original article

Effects of ambient air pollution on pulmonary function among schoolchildren

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ABSTRACT

Literature has shown adverse effects of ambient air pollution exposure on various asthma related outcomes in childhood. However, the associated evidence on pulmonary function effects is still inconsistent.

We conducted a population-based study comprised of seventh-grade children in 14 Taiwanese communities. Pulmonary function tests and questionnaires were completed on 3957 subjects. We evaluated the effects of ambient air pollution exposures based on the data collected in 2005–2007 by existing air monitoring stations. Multiple linear mixed effect models were fitted to estimate the relationship between community pollutant levels and pulmonary function indices. After adjustment for individual-level confounders, pulmonary function differed only slightly between communities with different levels of air pollution. We found greater effects of ambient air pollutants on pulmonary function for boys than for girls. Among boys, traffic-related pollutants CO, NOx, NO_2, and NO were generally associated with chronic adverse effects on FVC and FEV_1, and subchronic adverse effects mainly on maximal mid-expiratory flow (MMEF) and peak expiratory flow rate. Among girls, only NOx and NO_2 showed subchronic adverse effects on MMEF. Although effect estimates of SO_2, PM_{10}, and $PM_{2.5}$ were generally negative for boys, none achieved statistical significance.

Our data suggests that ambient traffic-related pollution had chronic adverse effects on pulmonary function in schoolchildren, especially for boys.

Introduction

Many studies have reported adverse effects of ambient air pollution on various aspects of respiratory health in children, including asthma exacerbations (Schildcrout et al., 2006), doctor-diagnosed asthma (Brauer et al., 2002; Hwang et al., 2005; Shima et al., 2003), and asthmatic symptoms (Braun-Fahrlander et al., 1997; Morgenstern et al., 2007). Pulmonary function as a sensitive marker of respiratory health effects of the lower airway has been documented in previous studies (Anon., 1996a,b). Most major pollutants can alter pulmonary function in addition to other health effects when the exposure concentrations are high. However, some studies have indicated no association between ambient air pollution and pulmonary function, especially in ambient low-dose exposure (Brunekreef et al., 1995; Dockery et al., 1989).

Although the problems of air pollution in Taiwan are relatively severe, it was not until recent years that the respiratory health effects associated with air pollution were reported (Chen et al., 1999; Ho et al., 2007; Hwang et al., 2005; Yang et al., 2007; Yu et al., 2005). From our previous Taiwanese ISAAC study, chronic exposure to traffic-related air pollutants was found to be associated with the risk of asthma in schoolchildren (Hwang et al., 2005). We did not collect pulmonary function data at that time and some important indoor exposures were not included in the questionnaire. In present study, we used the data from Taiwan Children Health Study (TCHS) to investigate the chronic adverse effects of ambient air pollution on pulmonary function. In present study, air monitoring data was applied to elaborate the relationship of different sources of pollutants with four kinds of pulmonary indices in Taiwanese children.

Methods

Study design

Taiwan Children Health Study (TCHS) was based on a multipurpose nationwide design that focused on CO, NOx, O_3, SO_2, and particulate matters as outdoor pollutants of primary interest (Hwang and Lee, 2010). Communities of Taiwan were selected

Abbreviations: CO, carbon monoxide; NOx, nitrogen oxides; NO, nitrogen monoxide; NO_2, nitrogen dioxides; O_3, ozone; SO_2, sulfur dioxide; $PM_{2.5}$, particulate matter with 50% cut-off aerodynamic diameter of 2.5 μm; PM_{10}, particulate matter with 50% cut-off aerodynamic diameter of 10 μm; SD, standard deviation; IQR, interquartile range; FVC, functional vital capacity; FEV_1, forced expiratory volume in 1 s; MMEF, maximal mid-expiratory flow; PEF, peak expiratory flow rate.

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with the aim of maximizing the variability and minimizing the correlations in criteria outdoor pollutants based on historic routine air monitoring data. In communities with pollution patterns of interest, neighborhoods with stable, largely middle-income populations, ethnically representative of Taiwan as a whole, were identified from 2004 census data. To address community-level sources of variability, we sought to maximize the number of participating communities within existing financial constraints. School district representatives in participating communities were consulted to identify suitable schools, based on demographic stability, likely parental cooperation, and absence of local pollution sources. Presentations were made to school administrators, teachers, and students to explain the study aims. Finally, our study population comprised subjects from 14 communities covering diverse parts of Taiwan, which was representative of Taiwanese middle-school children.

A total of 4765 seventh-grade children were recruited from public schools in 14 communities in 2007. The questionnaire was distributed to all schools in September, and subjects were arranged to complete pulmonary function tests in the following two weeks. Questionnaire responses by parents or guardians were used to categorize children's basic information, medical history, family history, personal habits, housing characteristics, and environmental conditions. In any classroom targeted for participation, every student was invited to volunteer. In each school, science, health, or physical education classes were targeted, excluding any special classes for gifted or learning-disabled subjects. The study protocol was approved by the Institutional Review Board at our university hospital, and it complied with the principles outlined in the Helsinki Declaration (Helsinki, 1990).

Air monitoring data

Complete monitoring data for outdoor pollutants carbon monoxide (CO), nitrogen oxides (NOx), nitrogen monoxide (NO), nitrogen dioxides (NO_2), ozone (O_3), sulfur dioxide (SO_2), particulate matter with 50% cut-off aerodynamic diameter of 2.5 μm ($PM_{2.5}$), and 10 μm (PM_{10}) were collected from Taiwan Environmental Protection Agency (EPA) air monitoring stations in 14 communities. Concentrations of each pollutant were measured continuously and reported hourly – CO by non-dispersive infrared absorption, NOx by chemiluminescence, O_3 by ultraviolet absorption, SO_2 by ultraviolet fluorescence, and particulate matters by beta-gauge. Chronic values of pollutants were defined as annual average concentrations calculated from the monthly averages of the year 2005–2007. Subchronic values were defined as monthly averages of July to September 2007.

Pulmonary function test (PFT)

Pulmonary function tests were performed during the morning hours in indoor buildings to avoid daily and annual peak air pollution levels, which occur most often during summer and autumn afternoon. The children who returned parental questionnaire were included. After excluding subjects with incomplete questionnaire, recent symptomatic upper respiratory infections, or other acute pulmonary or cardiac diseases, the remaining 4355 children were eligible for pulmonary function tests.

Each subject was asked to perform three satisfactory blows, defined as both of the two largest functional vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) agreeing within 200 ml, extrapolation volume less than 150 ml or 5% of FVC, and forced expiratory time exceeding 6 s, not less than 5 s. These criteria are based on American Thoracic Society recommendations, updated in 2005, modified for children. No more than 5 blows were attempted per time, no more than two times were asked per child. Resting for more than 10 min was required for every subject to prevent exercise bias. To predict subjects' pulmonary function, height, and weight were measured at the time of testing, using the same device, with shoes and coats removed, while age, sex, and other potential confounders were determined from parents' questionnaire responses. Two fully trained technicians performed PFT, using two identical spirometers (Chestgraph HI-101, CHEST M.I., Inc.). Each school was visited for one time. Spirometers' calibrations were checked before, during, and after every morning's testing using 1 L flow-volume syringes.

Statistical analysis

To investigate the relationship between PFT and air pollutants, we used multiple linear mixed effect models (PROC MIXED) for analyzing two-stage hierarchical data. The models assume two sources of variation: the variation among subjects in the first stage, part of which could be explained by the individual characteristics, and the variation among communities in the second stage, part of which could be explained by variables measured at community level. In the analyses we assumed that (i) the outcome variable follows normal distribution; (ii) intercept terms are random at the community level; and (iii) all the explanatory variables are fixed effects. We fitted linear regression models to adjust for personal variables such as sex, age, height, and weight as well as those potential confounders described in Table 3 for each PFT index, including FVC, FEV_1, maximal mid-expiratory flow (MMEF), or peak expiratory flow rate (PEFR). Multiple linear regression models were utilized to determine which potential confounder was significantly correlated with PFT indices. The potential confounders with the $p < 0.15$ for a given PFT index were included in all subsequent models of pollutant effects.

Since the numerical scale of effect estimates is different among the various pollutants, we standardize each to its inter-quartile range, along with their 95% CIs, across communities. Subjects with missing covariate information were included in the model using missing indicators (Huberman and Langholz, 1999). The above models were applied to all subjects in the dataset and to subsets stratified by sex. Since the pollutant measures represent outdoor ambient levels, we also tried to determine whether the habit of outdoor activity modified the PFT–pollutant relationship. At study entry, subjects' parents were asked in questionnaire if their children have the habit to do outdoors activity. Responses to this question were utilized to stratify subjects into either the "more outdoor activity" group or "less outdoor activity" group. Regression analyses of pollutant effects were then performed separately for each of the two groups. Using similar methodology, we also stratified our population based on habit of air cleaner use and doctor-diagnosed asthma. All analyses were performed by SAS software version 9.1 (SAS Institute, Gary, NC, USA) and assumed a 0.05 significant level based on a two-sided estimate.

Results

The overall response rate in TCHS was 86.5%. After dropping out subjects absent in the testing day, with active smoking habits, poor compliance or unsatisfactory blow, our study finally comprised 3957 (90.9%) children with complete pulmonary function data. All subjects were 12–13 years of age and of the same Han Chinese ethnic origin.

Table 1 summarizes the distribution of air pollutants from monitoring stations in 14 communities. Means and standard deviations of pulmonary function indices among seven-grade schoolchildren of our study show normal distribution (Table 2). We could find that boys had higher FVC, FEV_1, MMEF, and PEFR than girls. Table 3 presents the correlation between potential confounders and pul-

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Table 1
Distribution of air pollutants data from 14 monitoring stations in Taiwan.

		Mean	SD	Maximum	Minimum	Range	25 percentile	75 percentile	IQR
CO (ppm)	Chronic	0.53	0.12	0.78	0.30	0.47	0.46	0.58	0.12
	Subchronic	0.40	0.11	0.68	0.23	0.44	0.35	0.46	0.12
NOx (ppb)	Chronic	23.99	7.25	36.99	13.34	23.65	17.88	29.32	11.45
	Subchronic	17.39	6.04	28.84	9.03	19.81	11.74	21.95	10.22
NO (ppb)	Chronic	5.85	2.37	10.34	2.52	7.82	4.18	6.83	2.66
	Subchronic	4.19	1.89	8.06	1.74	7.25	2.73	5.12	2.39
NO_2 (ppb)	Chronic	18.13	5.02	26.84	10.80	16.04	13.63	22.49	8.86
	Subchronic	13.21	4.40	20.78	7.01	13.77	9.32	17.22	7.91
O_3 (ppb)	Chronic	27.21	3.90	37.01	20.95	16.06	24.93	28.74	3.80
	Subchronic	25.93	3.90	31.90	18.87	13.03	23.07	28.60	5.53
SO_2 (ppb)	Chronic	4.68	2.20	10.09	2.16	7.92	3.24	5.54	2.30
	Subchronic	3.90	1.48	7.87	1.87	6.00	2.97	4.65	1.68
PM_{10} ($\mu g/m^3$)	Chronic	60.84	17.07	88.97	36.72	52.25	47.70	76.63	28.93
	Subchronic	43.24	6.89	54.67	30.33	24.33	37.67	47.50	9.83
$PM_{2.5}$ ($\mu g/m^3$)	Chronic	34.50	10.67	51.94	19.97	31.97	26.13	44.67	18.54
	Subchronic	24.88	4.70	31.00	17.00	14.00	20.75	29.58	8.83

Definition of abbreviations: SD = standard deviation; IQR = inter-quartile range; PM_{10} = particulate matter with 50% cut-off aerodynamic diameter of 10 μm.
Chronic values are defined as average concentrations calculated from the monthly averages from year 2005 to 2007. Subchronic values are defined as monthly averages from July 2007 to September 2007.

Table 2
Means and standard deviations of pulmonary function indices among seven-grade schoolchildren in our study.

	All subjects (n = 3957)		Boys (n = 1989)		Girls (n = 1968)	
	Mean	SD	Mean	SD	Mean	SD
FVC (ml)	2758.5	511.0	2945.4	563.4	2569.0	364.3
FEV_1 (ml)	2500.0	446.0	2630.4	506.8	2367.7	324.9
MMEF (ml)	3109.8	728.6	3163.0	803.4	3055.8	639.7
PEFR (ml)	4841.2	1225.9	5229.4	1289.0	4447.4	1017.1

Definition of abbreviations: SD = standard deviation; FVC = functional vital capacity; FEV_1 = forced expiratory volume in 1 s; MMEF = maximal mid-expiratory flow; PEFR = peak expiratory flow rate.

monary function results. Older age, higher height and higher weight were uniformly associated with pulmonary function increments. Children with higher parental education level had increased FVC and PEFR. In the analyses of pollutant effects, items with the $p < 0.15$ in each pulmonary function index were included in the first stage model. A considerable amount of variation was accounted for by these factors with R^2 of 0.90 for FVC and 0.88 for FEV_1. The adjusted values of pulmonary function indices for the 14 communities were computed based on the regression models shown in Table 3. For all subjects, there was a statistically significant difference of all pulmonary function indices across the communities. When all subjects were divided by sex, the boys showed greater community variation than girls.

The relationships between pulmonary function indices and ambient air pollutants are presented in Table 4 for all subjects, boys and girls. In general, we found greater effects of outdoor air pollutants on pulmonary function indices for boys than for girls. Among boys, CO was significantly associated with chronic and subchronic adverse effects on FVC, FEV_1, MMEF, and PEFR; NOx, NO, and NO_2 were associated with chronic adverse effects on FVC and FEV_1; NO_2 showed similar chronic and subchronic adverse effects on MMEF. Although effect estimates of SO_2, PM_{10}, and $PM_{2.5}$ were generally negative for boys, none achieved statistical significance. Among girls, only NOx and NO_2 showed subchronic adverse effects on MMEF (Table 4).

We further stratified the data by outdoor activity according to the questionnaires to determine whether the effects of outdoor CO, NOx, NO, and NO_2 are greater in the subjects who spend more time outdoors (Table S1). We found effect estimates were generally larger for those spending more time outdoors in both sexes. For boys with more outdoor activity, NOx, NO, and NO_2 had statistically significant chronic effects on FVC and FEV_1. For girls with more outdoor activity, NOx and NO were associated with subchronic adverse effects on FEV_1 and MMEF; NO_2 was significantly associated with subchronic adverse effects on MMEF. For the stratification anal-

Table 3
Regression coefficients of covariates on pulmonary function indices in our population.

	FVC		FEV_1		MMEF		PEFR	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Age (year)	181.4$^{\$}$	(155.8, 207.0)	173.4$^{\$}$	(150.3, 196.5)	221.1$^{\$}$	(181.1, 261.0)	356.8$^{\$}$	(292.3, 421.3)
Girls	387.0$^{\$}$	(358.6, 415.4)	274.2$^{\$}$	(248.5, 299.8)	129.9$^{\$}$	(85.4, 174.4)	819.3$^{\$}$	(747.9, 890.7)
Height (cm)	2.4$^{\$}$	(0.9, 3.9)	2.1$^{\$}$	(0.7, 3.4)	1.9*	(−0.5, 4.3)	5.1$^{\$}$	(1.2, 8.9)
Weight (kg)	2.6$^{\$}$	(1.8, 3.4)	1.7$^{\$}$	(1.0, 2.4)	0.8	(−0.4, 2.0)	2.1$^{\#}$	(0.1, 4.0)
Parents education level (>9 years)	38.4$^{\#}$	(0.2, 76.6)	31.0	(−3.4, 65.4)	19.8	(−39.9, 79.5)	99.2$^{\#}$	(3.2, 195.3)
Mother smoking during pregnancy	35.2	(−36.5, 107.0)	32.5	(−32.2, 97.2)	70.4	(−42.2, 182.9)	7.3	(−173.0, 187.6)
Passive smoking at home	11.1	(−17.7, 39.9)	10.6	(−15.4, 36.6)	6.2	(−39.4, 51.8)	9.2	(−63.2, 81.6)
Dog at home	11.2	(−20.2, 42.7)	15.9	(−12.5, 44.2)	37.8	(−12.3, 88.0)	15.1	(−64.0, 94.1)
Cat at home	−13.8	(−76.4, 48.8)	14.4	(−42.1, 70.8)	65.7	(−110.8, 242.2)	77.1	(−80.2, 234.3)
Visible mould at home	−4.3	(−34.2, 25.7)	1.2	(−25.8, 28.2)	6.8	(−40.1, 53.8)	25.9	(−49.4, 101.2)
Water damage at home	−7.3	(−53.5, 38.9)	−13.6	(−55.3, 28.1)	−22.3	(−94.8, 50.3)	−42.8	(−159.0, 73.4)

For definition of abbreviations, see Table 2.
All models are adjusted for communities.
Factors with $p < 0.15$ are adjusted for each other in each pulmonary function index; remaining variables are adjusted only for the variables with $p < 0.15$.
Factors with $p < 0.15$ are included in the final adjustment models for each pulmonary function index.
* $p < 0.15$.
$^{\#}$ $p < 0.05$.
$^{\$}$ $p < 0.01$.

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Table 4
Changes in pulmonary function indices (ml) per inter-quartile range elevation of each air pollutant.

			All subjects (n = 3957)		Boys (n = 1989)		Girls (n = 1968)	
			Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
FVC	CO	Chronic	−40.0#	(−64.9, −15.0)	−56.8#	(−87.1, −26.4)	−20.8	(−47.1, 5.5)
		Subchronic	−44.1#	(−76.0, −12.3)	−60.3#	(−101.0, −19.5)	−24.4	(−56.1, 7.3)
	NOx	Chronic	−79.1*	(−140.3, −17.9)	−99.8*	(−181.9, −17.7)	−50.4	(−108.5, 7.8)
		Subchronic	−73.2	(−148.2, 1.8)	−81.4	(−183.6, 20.8)	−54.0	(−120.2, 12.3)
	NO	Chronic	−44.9*	(−84.5, −5.4)	−54.8*	(−108.3, −1.3)	−30.3	(−66.6, 6.0)
		Subchronic	−43.4	(−93.7, 7.0)	−45.7	(−114.5, 23.1)	−35.4	(−78.5, 7.7)
	NO_2	Chronic	−94.5*	(−166.6, −22.3)	−120.7*	(−216.8, −24.7)	−58.7	(−127.8, 10.5)
		Subchronic	−75.1	(−153.5, 3.3)	−85.1	(−191.2, 21.1)	−53.0	(−122.9, 16.9)
	O_3	Chronic	22.9	(−18.6, 64.5)	46.7	(−3.0, 96.4)	0.4	(−36.7, 37.5)
		Subchronic	−6.2	(−74.9, 62.5)	10.4	(−79.0, 99.7)	−16.1	(−73.9, 41.8)
	SO_2	Chronic	−14.6	(−60.8, 31.7)	−3.6	(−65.5, 58.3)	−21.8	(−60.2, 16.6)
		Subchronic	−7.1	(−64.5, 50.2)	18.3	(−56.5, 93.0)	−25.6	(−72.5, 21.2)
	PM_{10}	Chronic	5.1	(−75.3, 85.6)	7.3	(−97.7, 112.4)	6.1	(−62.3, 74.6)
		Subchronic	−6.2	(−75.9, 63.5)	−6.8	(−97.7, 84.1)	−4.0	(−63.5, 55.5)
	$PM_{2.5}$	Chronic	−3.3	(−82.2, 75.6)	−5.1	(−108.2, 98.0)	2.5	(−64.6, 69.7)
		Subchronic	−7.1	(−94.4, 80.2)	−13.3	(−127.0, 100.5)	5.2	(−69.0, 79.4)
FEV_1	CO	Chronic	−33.3#	(−55.5, −11.2)	−46.8#	(−72.0, −21.6)	−17.4	(−42.6, 7.7)
		Subchronic	−37.8#	(−65.3, −10.2)	−49.6#	(−83.4, −15.8)	−22.4	(−52.2, 7.4)
	NOx	Chronic	−69.4#	(−121.7, −17.1)	−83.9*	(−151.4, −16.5)	−46.3	(−101.0, 8.3)
		Subchronic	−70.3*	(−132.4, −8.2)	−71.9	(−155.1, 11.3)	−57.5	(−117.6, 2.5)
	NO	Chronic	−39.2*	(−73.2, −5.2)	−45.4*	(−89.6, −1.1)	−27.7	(−61.9, 6.5)
		Subchronic	−38.9	(−81.8, 4.0)	−35.5	(−92.8, 21.7)	−36.5	(−75.9, 2.9)
	NO_2	Chronic	−83.2#	(−144.7, −21.6)	−102.3*	(−180.8, −23.8)	−54.1	(−119.1, 10.9)
		Subchronic	−73.8*	(−138.2, −9.5)	−78.4	(−163.8, 7.1)	−57.4	(−120.7, 5.9)
	O_3	Chronic	21.4	(−14.0, 56.9)	43.1*	(4.0, 82.2)	1.0	(−33.8, 35.8)
		Subchronic	1.6	(−57.7, 61.0)	18.7	(−54.3, 91.7)	−8.7	(−63.4, 46.0)
	SO_2	Chronic	−13.3	(−53.2, 26.7)	−2.2	(−53.6, 49.2)	−19.9	(−56, 16.1)
		Subchronic	−11.3	(−60.4, 37.9)	14.2	(−47.8, 76.2)	−29.1	(−71.9, 13.8)
	PM_{10}	Chronic	7.6	(−61.6, 76.8)	8.1	(−78.8, 95.0)	11.6	(−52.4, 75.5)
		Subchronic	−6.6	(−66.7, 53.5)	−10.1	(−85.2, 65.0)	−0.8	(−56.5, 55.0)
	$PM_{2.5}$	Chronic	1.2	(−66.8, 69.2)	−1.2	(−86.6, 84.1)	9.1	(−53.6, 71.7)
		Subchronic	−7.2	(−82.4, 68.0)	−14.7	(−108.7, 79.2)	8.1	(−61.4, 77.5)
MMEF	CO	Chronic	−40.2	(−80.4, 0.0)	−52.7*	(−97.1, −8.4)	−25.4	(−71.5, 20.8)
		Subchronic	−50.5*	(−97.9, −3.1)	−59.4*	(−113.6, −5.1)	−38.8	(−92.5, 14.8)
	NOx	Chronic	−92.1*	(−181.8, −2.4)	−101.2	(−206.7, 4.4)	−74.2	(−174.5, 26.1)
		Subchronic	−117.1*	(−213.2, −21)	−108.5	(−227.5, 10.5)	−116.0*	(−219.3, −12.7)
	NO	Chronic	−52.5	(−109.6, 4.5)	−54.4	(−122.2, 13.4)	−45.2	(−107.5, 17.2)
		Subchronic	−59.5	(−127.9, 8.9)	−47.5	(−131.0, 36.0)	−66.5	(−136.7, 3.8)
	NO_2	Chronic	−110.1*	(−216, −4.3)	−123.9*	(−247.5, −0.2)	−86.1	(−205.2, 33.0)
		Subchronic	−126.6*	(−224.7, −28.5)	−122.4*	(−243.2, −1.5)	−120.4*	(−228.2, −12.6)
	O_3	Chronic	36.5	(−18.8, 91.8)	67.0*	(11.7, 122.4)	10.1	(−51.7, 71.8)
		Subchronic	30.7	(−60.8, 122.3)	61.4	(−38.8, 161.7)	11.9	(−85.5, 109.3)
	SO_2	Chronic	−11.7	(−75.7, 52.2)	1.3	(−73.6, 76.2)	−18.5	(−85.1, 48.2)
		Subchronic	−24.1	(−101.2, 53.1)	8.8	(−82.1, 99.7)	−48	(−125.5, 29.5)
	PM_{10}	Chronic	36.2	(−71.2, 143.5)	31.7	(−92.8, 156.3)	49.9	(−61.3, 161.2)
		Subchronic	2.9	(−91.9, 97.8)	−6.7	(−115.6, 102.2)	17.6	(−81.6, 116.8)
	$PM_{2.5}$	Chronic	28.9	(−77.0, 134.7)	23.6	(−99.1, 146.3)	44.6	(−64.8, 154.0)
		Subchronic	0.9	(−117.8, 119.6)	−8.4	(−144.8, 127.9)	22.5	(−101.3, 146.2)
PEFR	CO	Chronic	−76.1	(−161.3, 9.2)	−107.2*	(−202.6, −11.8)	−40.8	(−128.7, 47.1)
		Subchronic	−99.0	(−198.6, 0.6)	−126.0*	(−240.8, −11.2)	−66.2	(−168.4, 36.0)
	NOx	Chronic	−167.2	(−359.3, 24.9)	−200.0	(−427.5, 27.4)	−119.5	(−311.7, 72.6)
		Subchronic	−224.7*	(−429.4, −20)	−229.5	(−483.3, 24.3)	−201.5*	(−400.9, −2.0)
	NO	Chronic	−96.1	(−217.2, 25)	−112.3	(−256.4, 31.7)	−71.8	(−191.2, 47.6)
		Subchronic	−136.8	(−274.5, 0.9)	−145.2	(−312.9, 22.6)	−120.0	(−253.6, 13.7)
	NO_2	Chronic	−199.0	(−426.3, 28.2)	−240.1	(−508.4, 28.3)	−139.9	(−367.8, 88.0)
		Subchronic	−227.7*	(−443.3, −12)	−228.6	(−495.2, 37.9)	−206.1	(−415.1, 2.9)
	O_3	Chronic	59.8	(−58.5, 178.0)	116.1	(−11.8, 244)	8.4	(−108.5, 125.4)
		Subchronic	58.9	(−132.5, 250.4)	118.0	(−100.2, 336.1)	16.6	(−167.8, 200.9)
	SO_2	Chronic	−19.9	(−152.0, 112.2)	−12.9	(−170.7, 144.9)	−19.4	(−145.1, 106.4)
		Subchronic	−42.8	(−202.7, 117.1)	−6.3	(−198.6, 186.0)	−67.7	(−216.7, 81.4)
	PM_{10}	Chronic	121.2	(−94.3, 336.7)	124.7	(−133.1, 382.5)	128.4	(−74.8, 331.6)
		Subchronic	52.3	(−141.9, 246.5)	54.0	(−175.5, 283.5)	55.5	(−128.8, 239.8)
	$PM_{2.5}$	Chronic	104.0	(−110.0, 318.1)	102.7	(−153.1, 358.5)	117.6	(−83.0, 318.2)
		Subchronic	77.2	(−165.1, 319.5)	86.8	(−109.4, 373)	82.6	(−146.8, 312)

For definition of abbreviations, see Table 2.
Single pollutant models are adjusted for potential confounders described in Table 3.
Models for girls and boys are adjusted for the same factors except sex.
* $p < 0.05$.
# $p < 0.01$.

yses by household air cleaner use (Table S2), outdoor pollutants showed greater effects on those without air cleaner use at home. For boys without air cleaner use, CO, NOx, and NO_2 showed significantly adverse effects on FVC, FEV_1, and PEFR. For girls without air cleaner use, NO was associated with subchronic adverse effects on FEV_1 and MMEF; NO_2 was significantly associated with subchronic adverse effects on MMEF and PEFR.

Discussion

Our population-based epidemiologic study in 14 Taiwanese communities was designed to have adequate power for identifying respiratory effect of specific ambient air pollutant. It showed that traffic-related pollutants CO, NOx, NO_2, and NO had chronic adverse effects on pulmonary function in children. Deficits in pulmonary function indices were not significantly related to the ambient levels of O_3, SO_2, $PM_{2.5}$, and PM_{10}. After adjustment for individual-level confounders, pulmonary function differed only slightly between communities with different levels of air pollution. These results support recent cohort data in Southern California demonstrating that exposure to pollution from traffic has adverse effects on children's pulmonary function development (Gauderman et al., 2004, 2007).

Age, sex, height, weight, and active smoking habits were constitutionally associated with pulmonary function. We found that children with high parental education level were associated with better pulmonary function (Table 3), which was consistent with a previous study from United States (Harik-Khan et al., 2004). We minimized interference from these confounders by stratifying further analyses by sex, and adjusting factors with the $p < 0.15$ by regression models. Because the prevalence of active smoking (0.7%) was too low for stratification analyses in our data, we excluded subjects with active smoking habits for further analyses. The study communities were located in different regions of Taiwan and therefore exhibited differences in indoor residential factors. Dog/cat ownership, visible mould at home, and water damage did not show significant influence on children's pulmonary function and were not treated as confounders in our further regression models.

Our study indicated that chronic exposure to ambient NOx and CO significantly decreases pulmonary function in children. These findings are in concordance with several previous epidemiologic studies concerning chronic effects of ambient air pollution from Italy (Rosenlund et al., 2009), Finland (Timonen et al., 2002), and California (Peters et al., 1999). In present data, we found consistent effects of NOx and CO on FVC and FEV_1 that represent central airways, whereas the effects on MMEF and PEFR that provide information primarily on damage of the peripheral airways was more limited (Table 4). Outdoor NO_2 is strongly influenced by local traffic density (Jerrett et al., 2005). From our prior study in Taiwan, ambient NOx and CO were found to be highly correlated and might serve as indicators of traffic-related air pollution (Lee et al., 2008). Similarly, another recent cohort study from California revealed an adverse effect of prenatal exposure to NO_2 and CO on pulmonary function in asthmatic children (Mortimer et al., 2008).

Air pollution can induce oxidative stress in the respiratory tract resulting in airway inflammation (Cesaroni et al., 2008; Li et al., 2003). Chronic airway inflammation could produce the decreases in pulmonary function indices and the central airways seem to be mainly affected given the stronger signal that we detected for FVC in the present study. Plausible mechanisms of NO_2 pulmonary toxicity have been well described (Persinger et al., 2002) and may contribute to part of our findings. However, in human exposure studies, adverse pulmonary effects of NO_2 have generally been demonstrated at levels of exposure a magnitude higher than reported here (Kraft et al., 2005). The low ambient NO_2 levels we found are more likely to have served as a surrogate for traffic-related air pollutants. Although it is difficult to discuss etiological mechanisms in our cross-sectional design, we believe these pollutants may be causally related to pulmonary function through oxidative stress responses induced by pollutants highly correlated with NO_2 (Li et al., 2003; Seaton and Dennekamp, 2003).

Exposure to particulate air pollution has been found to be associated with small airway remodeling (Churg et al., 2003), pulmonary function deterioration (Lewis et al., 2005; Trenga et al., 2006), and impaired pulmonary function growth in children (Gauderman et al., 2004). Effects of ambient O_3 were also reported on FVC and FEV_1 decrements (Chen et al., 1999; Stern et al., 1994). However, the present data showed no significant relationship between pulmonary function indices and ambient levels of O_3, SO_2, and particulate matters (Table 4). Similar with our findings, some epidemiologic studies failed to show significant effects of ambient O_3 and particulate matters in children (Dockery et al., 1989; Rabinovitch et al., 2004; Ware et al., 1986). The lack of association for these pollutants may be due to their low ambient levels (Hoek and Brunekreef, 1994).

We have minimized the possibility of acute effects by scheduling PFT to avoid daily variation of ambient air pollutants. A previous study of Californian children has showed that the acute effect of ambient NO_2 was about −0.4 ml/ppb in contrast to the chronic effect of −1.7 ml/ppb on morning FVC measurements (Linn et al., 1996). Our data also indicated that the chronic effect of NO_2 (−10.7 ml/ppb) was slightly larger than subchronic effect (−9.5 ml/ppb) on FVC. Although the chronic and subchronic concentration of NO_2 was highly correlated in our data (correlation coefficient = 0.88), subchronic effects of NO_2 were significantly greater than chronic effects on MMEF and PEFR (Table 4). Because of variations in emission sources and measurement techniques, it is difficult to compare pollutants concentrations between studies from different countries.

When the subjects were divided by sex, our results showed statistically significant relationships between certain pollutant exposures and pulmonary function deficits, primarily among boys, which may have public health significance. Available literature on differences between sexes in response to air pollution did not provide a clear picture. A study of German children indicated more pronounced effects for boys (Ulmer et al., 1997) while a study in the Netherlands of traffic-related pollution showed stronger associations for girls (Brunekreef et al., 1997). We found a significantly greater effect of NO_2 on pulmonary function among boys than girls. The mechanism of such male-led susceptibility is not well understood. One possible explanation considered is that boys might have more extensive exposures because they are relatively active and spend more time outdoors and, therefore, are more influenced by air pollutants. Sex-differences in the pathogenesis of pulmonary function effects might be partly due to difference in lifestyle, hormonal factors, or differences in pulmonary growth physiology.

Our results showed that effects of CO, NOx, NO, and NO_2 were greater among children who spent more time outdoors (Table S1). This finding is consistent with a previous report indicating that chronic exposure to ambient air pollution was significantly associated with lower FVC and FEV_1 only among children with more outdoor activities (Peters et al., 1999). Numerous studies have demonstrated that ambient air pollution was associated with pulmonary function deterioration in children, especially in asthmatics (Delfino et al., 2004; Mortimer et al., 2002). Although the association between traffic-related air pollution and childhood asthma has been confirmed in our previous ISAAC study (Hwang et al., 2005), in present data, we could not find greater effects of air pollution among asthmatic children (Table S3). The phenomenon indicated the independent pathognomonic pathway of ambient air pollution on deteriorated pulmonary function in Taiwanese population,

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rather than through asthma. The exact reason is still unknown and warrants further investigations.

Large studies of prospective cohort design are better able to address health effects of chronic environmental exposures. TCHS was designed to be a longitudinally prospective study. We targeted all schoolchildren in the predefined classrooms/schools and the high response rate (90.9%) makes selection bias less likely happen. We do not think we have missed any important potential confounders in our analyses. Migrating from one community to another could lead to misclassification of exposure. However, errors in exposure assessment were likely to be random, which would reduce the magnitude of association, but would not introduce a positive bias in the associations. Measurements of ambient air pollutants were made by community-level monitoring stations. Bias could be introduced if differential changes of certain pollutants were found between communities, but annual mean pollutant concentrations seem rather stable in TCHS communities during recent years. There are variations of ambient concentrations within communities over which we have no control. However, most pollutants do not show seasonal variation greatly within communities, and air monitoring stations are likely to be a good representation of outdoor exposures in our study.

Conclusion

Traffic-related air pollutants (CO, NOx, NO, and NO_2) showed chronic and subchronic adverse effects on pulmonary function in children, especially for boys. The effects were larger in those spending more time outdoors and/or not using air cleaner at home. Children's individual exposure to air pollutants as well as measurements of time activity should be assessed in more detail to estimate the dose–response relationship precisely. Public health policy for reducing respiratory health burden may require a stronger focus on traffic-related air pollutants where children could gain significant benefits in Taiwan.

Ethical approval

The study was approved by the Institutional Review Board at our university hospital, and all procedures were done according to the research ethics of the Declaration of Helsinki.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijheh.2011.05.004.

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