Children's Respiratory Morbidity Prevalence in Relation to Air Pollution in Four Chinese Cities

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We examined respiratory health effects of long-term exposure to ambient air pollution in 7,621 schoolchildren residing in eight districts of four Chinese cities. The four cities exhibited wide between-city and within-city gradients in ambient levels of four size fractions of particulate matter [≤ 2.5 μm in aerodynamic diameter ($PM_{2.5}$), between 2.5 and 10 μm ($PM_{10-2.5}$), ≤ 10 μm (PM_{10}), and total suspended particulates (TSP)] and two gaseous pollutants (SO_2 and NO_x). Informed consent and written responses to questionnaires about children's personal, residential, and family information, as well as their health histories and status, were obtained with the help of the parents and the school personnel. We used a two-stage regression approach in data analyses. In the first-stage logistic regressions, we obtained logits of district-specific prevalence of wheeze, asthma, bronchitis, hospitalization for respiratory diseases, persistent cough, and persistent phlegm, adjusted for covariates representing personal, household, and family parameters. Some of these covariates were found to be risk factors of children's respiratory health, including being younger in the study group, being male, having been breast-fed, sharing bedrooms, sharing beds, room being smoky during cooking, eye irritation during cooking, parental smoking, and a history of parental asthma. In several of the second-stage variance-weighted linear regressions, we examined associations between district-specific adjusted prevalence rates and district-specific ambient levels of each pollutant. We found positive associations between morbidity prevalence and outdoor levels of PM of all size fractions, but the association appeared to be stronger for coarse particles ($PM_{10-2.5}$). The results also present some evidence that ambient levels of NO_x and SO_2 were positively associated with children's respiratory symptoms, but the evidence for these two gaseous pollutants appeared to be weaker than that for the PM. *Key words:* air pollution, children, China, particulate matter, respiratory health. *Environ Health Perspect* 110:961–967 (2002). [Online 14 August 2002]
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Health effects of exposure to ambient air pollutants [e.g., particulate matter (PM), sulfur dioxide (SO_2), nitrogen dioxide (NO_2)] have been investigated in numerous epidemiologic studies, mainly in North America and Europe. In general, these studies have presented evidence that exposure to certain ambient pollutants adversely affects public health, as summarized in several review articles (1–5). However, the available evidence remains subject to uncertainties due to various study limitations, including *a*) the simultaneous presence of highly intercorrelated pollutants; *b*) interference from confounding effects resulting from the ethnic, demographic, and other factors that influence susceptibility to pollution effects; and *c*) the lack of appropriate exposure ranges in cross-sectional studies (1).

The Chinese government and the U.S. Environmental Protection Agency (U.S. EPA) have jointly funded an epidemiologic study of children's and adults' respiratory health in relation to long-term exposure to ambient and indoor air pollution in urban and suburban districts of four Chinese cities: Lanzhou, Chongqing, Wuhan, and Guangzhou (for convenience, the study is called the Four Chinese Cities Study). These cities were chosen because they exhibited wide between-city gradients and within-city differences of ambient pollutant levels, thus offering a valuable epidemiologic opportunity for exposure–response assessment (6). The study included multiyear measurements of four size fractions of ambient PM—total suspended particulates (TSP), particles with aerodynamic diameter ≤ 10 μm (PM_{10}) and ≤ 2.5 μm ($PM_{2.5}$), and the coarse fraction of PM_{10} (diameters between 2.5 and 10 μm, $PM_{10-2.5}$)—and of SO_2 and oxides of nitrogen (NO_x). Ambient concentrations of these pollutants measured in each of the eight districts, along with geographic locations, climate, population density, and major indoor and outdoor pollution sources, have been reported in detail elsewhere (6). The Four Chinese Cities Study also provides an opportunity to study air pollution effects in urban and suburban residents of Chinese ethnicity. When this study was conducted (1993–1996), the vast majority of Chinese people usually had resided in their districts throughout their lifetimes. Therefore, the populations selected were appropriate for a study of health effects of long-term exposure. In this article, we specifically address the effects of ambient air pollutants and indoor air pollution sources as well as other lifestyle/household factors on respiratory morbidity prevalence in children living in the eight districts of the four Chinese cities.

Methods

Site selection and subject recruitment. The study districts were selected with the aims of maximizing the between-city and within-city concentration gradients in the ambient air pollutants of interest and of minimizing the correlation between district-specific ambient particulate and sulfur dioxide pollution. These aims were achieved by selecting an urban district and a suburban district in each of the four cities (6). Elementary school students and their families were chosen to provide the subject pool. The schools were all reasonably close to their districts' municipal monitoring stations, where ambient TSP, SO_2, and NO_x concentrations were measured (within 8 km for the Lanzhou suburban school and the Guangzhou suburban school and within 1.5 km for all the other schools). Subject eligibility was based on the following general inclusion criteria: Their families had no plans to move within next 3 years, and their homes were within 2 km of the schools.

Signed informed consent forms were obtained from the parents or guardians of all study children before their participation in the study.

Ambient air pollution measurement. The details on the air pollution measurements can be found in the previous report by Qian et al. (*6*). Briefly, concentrations of TSP, SO_2, and NO_x were obtained from municipal air pollution monitoring stations, because these regulated pollutants were routinely measured in all the study districts. Size-fractionated PM measurements were not available at these stations and therefore were specifically measured in the schoolyards. TSP concentrations were also measured in the schoolyards for comparison. Because data on health outcomes and other relevant parameters were collected from 1993 to 1996, we obtained data on SO_2, NO_x, and TSP measurements for these 4 years from the municipal monitoring stations. The schoolyard measurements, however, were made for only 2 years (1995 and 1996) because of financial and logistical limitations. The TSP, SO_2, and NO_x measurements at the municipal monitoring stations strictly followed the standard methods set by the State Environmental Protection Administration of China (*6,7*). In the schoolyards, concentrations of $PM_{2.5}$ and $PM_{10-2.5}$ were measured using dichotomous samplers (model 241; Sierra-Anderson, Atlanta, GA) provided by U.S. EPA with certification as reference sampling devices. Teflon filters were used in the dichotomous samplers to collect $PM_{2.5}$ and $PM_{10-2.5}$ samples. The PM sampling and filter weighing were done after rigid quality assurance procedures (*6*). PM_{10} concentrations were obtained by adding $PM_{2.5}$ concentrations and $PM_{10-2.5}$ concentrations.

Questionnaire survey. Cross-sectional information on residential history, lifestyles, household characteristics, and children's and parents' health histories was obtained through a questionnaire survey administered during 1993–1996. The survey instrument was a single detailed and standardized questionnaire adapted from the American Thoracic Society Epidemiologic Standardization Project questionnaire (*8*). The questionnaire and study procedures had been slightly modified in light of an earlier pilot study (*9,10*). The questionnaire was administered in Chinese and included detailed questions on date of questionnaire administration, date of birth, sex, breast-feeding, number of years lived in each residence, types and characteristics of dwelling, method of cooking and heating, location of kitchen, types of home ventilation devices (if any), home smokiness degree and eye irritation degree during cooking, history and current status of children's respiratory illnesses and symptoms, parental education levels, parental occupation levels, smoking status of parents and other household members, and parental respiratory health histories.

With the approval of the school administration, the study staff made presentations at the schools explaining the study to the students, their parents, and their teachers and principals. After obtaining signed parental consent forms for participation, the study staff distributed questionnaires. These were filled out by the parents either at school or at home. All questionnaire responses were recorded electronically in a database according to a standardized code and file structure.

Definitions of respiratory symptoms and illnesses. The following specific respiratory symptoms and illnesses were determined from questionnaire responses: *a*) wheeze: a yes answer to the question "Has this child's chest ever sounded wheezy or whistling when having a cold?" or a yes answer to the question "Has this child's chest ever sounded wheezy or whistling when not having a cold?" *b*) asthma: a yes answer to the question "Has a doctor ever diagnosed asthma in this child?" *c*) bronchitis: a yes answer to the question "Has a doctor ever diagnosed bronchitis in this child?" *d*) hospitalization due to respiratory diseases: a yes answer to the question "Has this child ever been hospitalized due to respiratory diseases?" *e*) persistent cough: the answers to several cough-related questions indicate that the study child has coughed for at least 1 month per year either with or apart from colds; *f*) persistent phlegm: the answers to several phlegm-related questions indicate that the study child has brought up phlegm or mucus from the chest for at least 1 month per year either along with or apart from colds.

Statistical analyses. To investigate relationships between respiratory morbidity prevalence and ambient air pollution levels, we used a two-stage regression approach similar to that used in previous studies [e.g., (*11–13*)]. In the first stage, we fitted a single logistic regression model for the prevalence rate of each morbidity outcome, including all selected covariates as independent variables and the district dummy variable. The covariates were selected based on epidemiologic literature and on results from exploratory stepwise logistic regressions, regarding which lifestyle/household variables were meaningfully associated with health outcomes. Interaction terms were not included because they were not statistically significant at $\alpha = 0.15$. The results from residual plots indicate that the models were fitted reasonably well.

In the first-stage logistic regressions, we obtained district-specific adjusted logits and the regression coefficients for the district variable, α_j for district j ($j = 1, \dots , 8$); we also obtained district-specific adjusted prevalence rates of each morbidity outcome. (All prevalence rates were adjusted to the grand means of covariate over the eight districts.) In the second-stage model, we regressed α_j on the district-specific ambient concentration (X_j) of each ambient air pollutant (one pollutant per model), using weighted linear regression with weights proportional to the inverse sum of between- and within-district variances (*14*). The expectation was that if there were an association between morbidity prevalence and pollutant level, there would be a nonzero slope in this model. We employed the standard *t*-test of zero slope for a regression model to determine whether the prevalence was correlated with the pollutant level. In addition, we translated the values of the slopes to prevalence odds ratios (ORs) and 95% confidence intervals (95% CIs), scaled so that the interquartile range (the distance from the 25th to the 75th percentile of district-specific concentrations) corresponds to one unit change.

Because the eight districts were nested in the four cities, we used additional second-stage models that tested separately for the between-city and within-city associations between prevalence and each pollutant (*13*). The models can be described with two-dimensional expression as follows: k denotes city ($k = 1, \dots , 4$) and l denotes urban or suburban district within a city ($l = 1, 2$); then $\alpha_{kl} = a + b_1 X_k + b_2 (X_{kl} - X_k) + e_{kb}$ where α_{kl} is the coefficient for district kl (similar to α_j in the first-stage model), X_k denotes the city-specific concentration for city k (the average of city k's two districts), X_{kl} denotes the pollutant concentration in district l of city k, and e_{kl} represents the error term. In this model, b_1 and b_2 represent between-city and within-city pollutant–outcome relationships, respectively. These coefficients were *t*-tested for zero slope and translated to ORs and 95% CIs.

Results and Discussion

Air pollution levels. Table 1 summarizes long-term average levels of ambient air pollutants—that is, 4-year arithmetic means of TSP, SO_2, and NO_x and 2-year arithmetic means of $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10}. Because the 4-year mean of TSP concentrations measured at the municipal monitoring stations agreed reasonably well with the 2-year mean of TSP concentrations measured in the schoolyards (*6*), the TSP values shown in Table 1 are the overall means of both the schoolyard data and the monitoring station data. Table 1 shows wide between-city and within-city gradients in long-term ambient levels of the measured pollutants. In addition, the gradient patterns for different pollutants were different across the eight districts; for example, $PM_{10-2.5}$ and TSP levels were the highest in the Lanzhou urban district, $PM_{2.5}$ and PM_{10} levels were highest in the Guangzhou urban district, SO_2 was the highest in the Chongqing urban district, and

NO_x was the highest in the Guangzhou urban district. The district-specific ambient pollutant levels were stable over several years before and during the study. These features of ambient air pollution were favorable for the study of effects of the individual pollutants (6).

Characteristics of subjects and households. Among 7,621 eligible children in the eight districts, 7,557 returned the questionnaires, making the overall participation rate 99.2%. District-specific participation rates and numbers of children in analysis are shown in Table 2, along with distributions of covariates included in the first-stage logistic regression models. Children who had less than 3 years of residence in their districts were excluded from further analyses. The overall exclusion rate was 2%. The children included in the analyses were between 5.4 and 16.2 years of age, with an overall female/male rate of 1:1 (3,695 girls, 3,697 boys). Given that the age range was wide and that age may have a significant impact on the prevalence of health outcomes in schoolchildren, we constructed several dummy variables for age, rather than using a continuous age variable in the logistic regression models (Table 2). Most children (72%) had been breast-fed.

House type, classified into four categories shown in Table 2, varied substantially across the eight districts: *dan-yuan-lou-fang* is an apartment unit in a multistory, multiunit building; "partially *dan-yuan-lou-fang*" refers to the situation that the study subjects had lived in such type of housing for part of their lifetimes; *ping-fang* is a one-story house typically with a small yard; and "other" refers to dormitory or any other unspecified house type. "Number of rooms" refers to how many rooms a household had. More children had never had their own bedrooms than children who had their own bedrooms for either entire or partial lifetimes. Most of the children had slept in their own beds at least for part of their lifetimes.

"Home coal use" refers to the use of coal in a household for cooking or space heating; it varied substantially across the eight districts, depending upon city, house type, and the local availability of fuel type. "Ventilation device use" refers to the use in a household of any of the following ventilation devices: exhaust fan, chimney, or fume hood (typically above a cookstove). "Home smokiness during cooking" and "eye irritation during cooking" were classified based on answers of the person who usually performed cooking tasks in a household to the question "How smoky does the home (excluding the kitchen) usually become during cooking?" and the question "When you cook food, how often do you get eye irritation from the smoke (not spices)?" respectively. These two variables are expected to be indicators of cooking smoke exposure. Parental smoking rates were high in all the study districts, with the overall rate being 75.2%. This resulted mainly from the high rates of paternal smoking; the rates of maternal smoking ranged from 0.4% to 2.5% in the eight districts (overall maternal rate = 1.2%).

"Mother's education level," "mother's occupation," and "father's occupation" are explained in Table 2. "Questionnaire respondent" was classified into two categories: mother versus other household member. Overall, in more than half of the households, mothers were the questionnaire respondents. Because the questionnaires were not all administered at the same time, year of questionnaire administration and season of questionnaire administration were controlled for in the logistic regressions. Table 2 shows that a vast majority of the questionnaires were administered in 1993 and during nonwinter seasons. The presence of paternal or maternal asthma has often been associated with children's respiratory health status (10–12,15). Therefore, parental asthma was considered as a covariate. The overall prevalence rate of parental asthma in the eight districts was 3.1%.

Prevalence rates of respiratory morbidity. After adjusting for all the covariates listed in Table 2, the district-specific prevalence of wheeze was 6.6–18.8%; asthma, 1.4–4.2%; bronchitis, 15.6–52.2%; hospitalization due to respiratory diseases, 7.7–26.7%; persistent cough, 5.7–14%; and persistent phlegm, 1.9–13.6% (Table 3). For comparison, the prevalence of wheeze in children reported in three studies in North America was 4–23% (11,12,14,16); in a study in Switzerland it was 3.7–9.1% (13); and in a study in Slovakia it was 10.6% (17). The prevalence of asthma in children reported in the three North American studies was 3–14.5% (11,12,14,16); in the Switzerland study and an Italian study it was 5.1–10.6% (13,18); and in the Slovakia study it was 3.9% (17). The prevalence of bronchitis in children reported in three North American studies was 3.6–13.1% (11,12,14); in the Switzerland study it was 5.7–27% (13); and in the Slovakian study it was 58.8% (17). The prevalence of persistent cough in children reported in the three North American studies was 3–9% (11,12,14); in the Switzerland study it was 4.7–19.2% (13); and in the Slovakian study it was 24.9% (17). The prevalence of persistent phlegm in children reported in one of the three North American studies was 1–5% (12) and in the Slovakian study was 5.1% (17). The prevalence of bronchitis and the prevalence of persistent cough in children appeared to be markedly higher in the Chinese and Slovakian cities where ambient pollution levels were also higher.

Effects of subject and household factors. The results of first-stage logistic regressions are shown in Table 4. Children of younger ages had higher adjusted prevalence rates of respiratory morbidities. Girls had lower prevalence of the respiratory morbidities (except persistent cough) than did boys. The age and sex effects observed in the present study are consistent with those observed in earlier studies (11,19).

Surprisingly, breast-feeding was associated with increased ORs for hospitalization and bronchitis. In examining the effects of house type, we found that "other," compared with *dan-yuan-lou-fang*, was more likely to be associated with lower prevalence of respiratory morbidity. Lower prevalence rates were associated with households with fewer rooms (fewer than three rooms). We could not find the underlying facts, based on our knowledge, to explain the unusual results on these three covariates (breast-feeding, house type, and number of rooms). Children who had never had their own bedrooms had a significantly higher adjusted prevalence rate of persistent cough, and those who had always slept in shared beds had higher adjusted prevalences of all the morbidity outcomes. These results occurred perhaps because sharing bedrooms or beds could increase the chances of being exposed to environmental tobacco smoke (ETS) and the like.

Table 1. District-specific ambient air pollutant concentrations (µg/m³): 2-year (1995–1996) arithmetic means for $PM_{2.5}$, $PM_{2.5–10}$, and PM_{10}, and 4-year (1993–1996) arithmetic means for TSP, SO_2, and NO_x.

City	District	$PM_{2.5}$	$PM_{10–2.5}$	PM_{10}	TSP	SO_2	NO_x
Guangzhou	Urban	150	87	237	276	55	230
	Suburban	66	41	107	196	40	69
Wuhan	Urban	73	56	129	232	72	123
	Suburban	52	30	81	214	15	38
Lanzhou	Urban	117	110	227	728	128	92
	Suburban	99	67	166	581	64	49
Chongqing	Urban	95	54	149	391	331	85
	Suburban	82	30	113	232	149	32
Grand mean		92	59	151	356	107	90
Range (max–min)		98	80	156	532	316	198
SD		31	28	56	198	101	64
Interquartile range[a]		39	42	87	263	91	64

Abbreviations: max, maximum; min, minimum.
[a]Range from 25th to 75th percentile of district-specific concentrations.

Home coal use was positively associated with wheeze, asthma, and bronchitis but negatively associated with hospitalization due to respiratory diseases, persistent cough, and persistent phlegm. Although an association between residential coal use and decreased lung function has been reported in Chinese children in an early study (20), the evidence for coal smoke effects on respiratory morbidities appeared to be weak in the present study. However, this finding should be interpreted with care, because there might be large errors associated with the exposure classification for coal smoke. For example, assessment of effects of home coal use, compared with no coal use, was based on an assumption that other types of cooking/heating fuels were not as polluting as coal. This assumption should

be validated with more refined exposure classification using information on all types of cooking fuels, all types of heating fuels, heating duration, and cooking frequencies, and the like. This is difficult to do with the current database.

The other possible reason evidence appears weak is that coal-generated indoor pollution could be readily diluted with high home air exchange rate because none of the residences in the study districts were built with an energy-conservation concept. Thus, residential coal burning might contribute more to community air pollution levels at the district level than to indoor air pollution levels at the individual house level. Interestingly, home smokiness during cooking and eye irritation during cooking were positively associated with

almost all respiratory outcomes, suggesting potential adverse effects of cooking fumes (smoke). However, the responses to these two variables could be highly subjective: the questionnaire respondents more susceptible to room smoke and eye irritation could be more likely to give positive answers to health outcome questions. The ORs of parental smoking were greater than 1 for all the morbidity outcomes. This finding is consistent with the findings in earlier studies that parental smoking is generally associated with higher prevalence rates of respiratory morbidity in schoolchildren (10,11,15,21).

Lower mother's education level appeared to be associated with lower prevalence rates. This might be due to possible survey bias, because households of lower maternal

Table 2. Information on subjects and distributions of covariates used in the first-stage logistic regression models.[a]

Characteristics	Guangzhou Urban	Guangzhou Suburban	Wuhan Urban	Wuhan Suburban	Lanzhou Urban	Lanzhou Suburban	Chongqing Urban	Chongqing Suburban
Participation rate (%)	99.3	98.8	99.3	96.9	99.5	99.5	99.3	99.6
Included in analysis[b] (person)	913	1,303	1,817	490	680	758	990	441
Age (%)								
5–7 years	31.9	32.4	13.0	16.7	50.7	52.6	25.7	38.5
8–9 years	30.0	26.2	43.9	37.8	22.4	17.3	52.8	50.1
10–11 years	23.5	29.6	33.5	28.0	25.0	26.9	21.3	11.3
≥ 12 years	14.6	11.8	9.6	17.6	1.9	3.2	0.2	0.0
Female (%)	48.8	50.4	50.8	49.0	50.6	45.6	51.2	52.6
Breast-fed (%)	69.1	70.8	63.8	84.1	74.3	86.4	59.8	66.4
House type (%)								
Dan-yuan-lou-fang	47.8	50.2	37.9	28.6	48.8	5.5	61.8	76.4
Partially dan-yuan-lou-fang	27.5	41.5	18.9	36.3	23.2	5.7	26.3	16.6
Ping-fang	17.7	6.8	15.0	24.7	27.5	88.8	9.9	4.3
Other (dormitory, etc.)	7.0	1.5	28.2	10.4	0.4	0.0	2.0	2.7
Number of rooms < 3 (%)	56.3	22.9	72.9	21.2	63.5	29.9	43.7	74.6
Sleeping in own or shared room (%)								
Ever in own room	27.7	50.8	25.8	39.8	30.4	23.4	49.3	58.0
Never in own room	72.3	49.2	74.2	60.2	69.6	76.6	50.7	42.0
Sleeping in own or shared bed (%)								
Ever in own bed	65.8	76.8	66.4	62.7	75.3	77.0	70.9	76.9
Never in own bed	34.2	23.2	33.6	37.3	24.7	23.0	29.1	23.1
Home coal use (%)	62.0	48.2	72.7	77.6	63.2	99.7	26.9	25.4
Ventilation device use (%)	76.9	91.1	38.6	53.5	77.2	97.0	69.3	70.7
Home smokiness during cooking (%)								
Not smoky	36.6	33.8	17.4	39.0	39.3	51.5	34.3	31.1
Lightly smoky	50.3	56.5	59.1	46.1	59.8	48.5	51.5	57.1
Moderately/heavily smoky	13.1	9.7	23.5	14.9	0.9	0.0	14.2	11.8
Eye irritation during cooking (%)								
Never or rarely irritating	44.3	47.5	20.4	41.0	22.7	22.3	31.5	31.7
Often or always irritating	55.7	52.5	79.6	59.0	77.3	77.7	68.5	68.3
Parental smoking (%)	69.0	58.8	84.2	79.6	76.2	82.1	75.4	80.3
Mother's education level (%)								
With/lower than primary schooling	6.6	5.3	3.8	26.8	9.3	31.5	3.2	2.3
Mother's occupation (%)								
Nonmanual laborer[c]	65.8	75.7	46.4	21.5	49.8	2.5	53.7	31.9
Father's occupation (%)								
Nonmanual laborer[c]	65.5	81.2	46.6	19.5	47.7	4.7	59.1	38.3
Questionnaire respondent (%)								
Mother	60.7	58.9	57.1	49.6	57.9	49.7	54.8	52.8
Year of questionnaire administration (%)								
1993	77.7	76.9	86.4	83.3	69.7	66.9	64.0	68.7
After 1993	22.3	23.1	13.6	16.7	30.3	33.1	36.0	31.3
Season of questionnaire administration (%)								
Winter	11.8	0.1	13.6	16.7	16.5	17.8	16.2	31.7
Parental asthma prevalence (%)	2.6	2.5	2.8	2.4	4.4	2.2	5.3	2.9

[a]Eight districts: 7,621 distributed questionnaires; 7,557 returned questionnaires; 7,392 included in analyses. [b]Excluded if a subject had stayed less than 3 years in his/her current residence. [c]Nonmanual laborer is similar to the so-called "white collar," such as teacher, doctor, business person, clerk, housewife (few cases); manual laborer is like the so-called "blue collar," such as factory worker, construction worker, building cleaning worker, farmer.

education levels have less access to health care facilities and usually tend to underreport symptoms. The children whose mothers were nonmanual laborers ("white-collar" workers) appeared more likely to be hospitalized for respiratory diseases than the children of the manual laborers ("blue-collar" workers), perhaps because the white-collar families had better access to hospital facilities. Parental occupation did not show a clear association with the other morbidity outcomes. Mothers were more likely to report a symptom or illness than were other questionnaire respondents. The time of questionnaire administration was associated with some of the morbidity outcomes, but the reason for this was not known. A reported parental history of

asthma was found to be a significant risk factor for all the morbidity outcomes, with ORs as large as 6.22 (for asthma). This finding in Chinese schoolchildren is in excellent agreement with findings from studies of U.S. schoolchildren (11,15).

Effects of ambient air pollutants. Table 5 presents the results from the second-stage weighted linear regressions. All six morbidity outcomes were positively associated with each of the four PM size fractions. The following associations achieved statistical significance ($p < 0.05$): bronchitis with $PM_{10-2.5}$, bronchitis with TSP, persistent cough with $PM_{10-2.5}$, persistent cough with TSP, persistent phlegm with $PM_{10-2.5}$, persistent phlegm with PM_{10}, and persistent phlegm and TSP. Three health

outcomes (wheeze, asthma, and persistent phlegm) were positively associated with ambient SO_2 concentrations. Only one outcome (persistent cough) was positively associated with ambient NO_x concentrations. No associations of prevalence with the gaseous pollutants SO_2 and NO_x were statistically significant.

When the overall associations derived from eight independent districts were broken down into between-city and within-city associations using the alternative second-stage models, both between-city and within-city positive associations remained for most of the PM–outcome pairs (Table 6). Within-city effects of $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} appeared to be stronger on wheeze and asthma. In contrast, between-city effects of all PM size fractions were stronger on bronchitis and hospitalization. Although SO_2 and NO_x had positive overall associations with only a few of the outcomes, their within-city associations were positive for all outcomes except persistent cough. This suggests the possible presence of some unknown between-city factors that might have overridden the effects of SO_2 and the effects of

Table 3. Adjusted prevalence rates (%) of respiratory morbidity by district, calculated using the grand mean of each covariate listed in Table 2.

Morbidity outcome	Guangzhou Urban	Guangzhou Suburban	Wuhan Urban	Wuhan Suburban	Lanzhou Urban	Lanzhou Suburban	Chongqing Urban	Chongqing Suburban
Wheeze	6.6	7.0	14.2	8.4	18.8	14.3	14.5	17.2
Asthma	2.2	1.6	2.5	1.4	4.2	1.7	2.3	3.3
Bronchitis	15.6	22.2	30.5	16.3	52.2	45.6	15.9	17.3
Hospitalization	9.9	15.9	21.2	14.5	26.7	14.1	7.7	12.4
Persistent cough	7.9	7.2	10.1	5.7	14.0	8.2	7.0	7.2
Persistent phlegm	2.7	1.9	3.8	2.4	13.6	6.2	3.0	2.4

Table 4. ORs of respiratory morbidity outcomes for the covariates included in the first-stage logistic regression models (see Table 2 for the distributions of the covariates).

Characteristics	Wheeze	Asthma	Bronchitis	Hospitalization	Chronic cough	Chronic phlegm
Age (ref: ≥ 12 years old)						
5–7 years old	1.60*	1.43	1.16	1.04	1.51*	1.28
8–9 years old	1.43*	1.41	1.28*	1.14	1.48*	1.33
10–11 years old	1.35**	1.19	1.14	1.16	1.20	1.05
Female (ref: male)	0.85*	0.67*	0.91**	0.82*	1.10	0.97
Breast feeding (ref: not breast-fed)	1.10	1.21	1.31*	1.28*	1.05	1.15
House type (ref: *dan-yuan-lou-fang*)						
Partially *dan-yuan-lou-fang*	1.07	1.14	0.96	0.91	0.97	0.72**
Ping-fang	1.10	1.08	0.91	0.94	0.96	1.01
Other (dorm, etc.)	0.74*	0.84	0.77*	0.93	0.78**	1.15
Number of rooms < 3 (ref: ≥ 3 rooms)	1.00	0.86	0.90**	0.81*	0.78*	0.74*
Sleeping in own or shared room (ref: ever in own room)						
Never in own room	0.99	1.19	1.00	1.01	1.25*	1.09
Sleeping in own or shared bed (ref: ever in own bed)						
Never in own bed	1.14**	1.08	1.07	1.08	1.08	1.13
Home coal use (ref: no coal use)	1.14	1.09	1.04	0.94	0.79*	0.92
Ventilation device use (ref: no device use)	0.98	1.18	1.00	0.97	0.95	1.11
Home smokiness during cooking (ref: not smoky)						
Lightly smoky	1.29*	1.21	1.20*	0.97	1.51*	1.43*
Moderately/heavily smoky	1.89*	1.61**	1.69*	1.12	2.89*	2.89*
Eye irritation during cooking (ref: never or rarely irritating)						
Often or always irritating	1.38*	1.34**	1.16*	1.24*	1.49*	1.56*
Parental smoking (ref: no parental smoking)	1.13	1.04	1.15*	1.15**	1.15	1.23
Mother's education level (ref: above primary schooling)						
With/lower than primary schooling	0.91	0.45*	0.84**	0.79**	0.56*	0.66**
Mother's occupation (ref: manual laborer)						
Nonmanual laborer	0.89	1.11	1.08	1.19*	1.00	0.99
Father's occupation (ref: manual laborer)						
Nonmanual laborer	1.13	1.01	1.10	1.09	0.97	0.98
Questionnaire respondent (ref: other than mother)						
Mother	0.90	1.02	1.16*	1.13**	1.15**	1.17
Year of questionnaire administration (ref: 1993)						
After 1993	0.99	0.92	1.18**	1.17	0.94	0.58*
Season of questionnaire administration (ref: other than winter)						
Winter	0.97	1.03	0.65*	0.75*	1.01	1.12
Parental asthma (ref: neither parent having asthma)	3.29*	6.22*	2.13*	1.66*	1.42**	1.78*

*$p < 0.05$; **$p < 0.15$.

NO_x in the schoolchildren living in the four geographically and climatically distinct cities (*22*). It is also possible that biases associated with the data pattern may have resulted in the within- and between-city differences, as shown in the following analyses.

Among the four cities, the Lanzhou urban district had highest TSP and $PM_{10-2.5}$ concentrations (Table 1) as well as highest adjusted prevalence rates of respiratory symptoms (Table 3). The findings of overall associations (between-city and within-city) may be biased by the specific close association between TSP/$PM_{10-2.5}$ and respiratory symptoms of Lanzhou. To test the robustness of the findings, we carried out the statistical analyses excluding the two Lanzhou districts. The new analyses show that the positive associations still remained for $PM_{2.5}$ with asthma, persistent cough, and persistent phlegm; for $PM_{10-2.5}$ with bronchitis, persistent cough, and persistent phlegm; for PM_{10} with persistent cough and persistent phlegm; and for TSP with wheeze and persistent phlegm. No changes were observed for any associations with SO_2. However, the new analyses found two additional positive associations for NO_x (with persistent cough and persistent phlegm). None of the associations (either positive or negative) reached statistical significance in the new analyses. Therefore, it appears that significant associations between coarse particles and children's respiratory symptom prevalence were mainly driven by high coarse particles levels and high prevalence rates in Lanzhou.

Of the four cities, the Guangzhou urban district had highest NO_x, PM_{10}, and $PM_{2.5}$ concentrations (Table 1) but had low adjusted prevalence rates of respiratory morbidity. To test whether the "protective" effect of NO_x on wheeze (Table 6) was caused by the data pattern of Guangzhou, we performed statistical analyses without the two Guangzhou districts and found that the new analyses had very little impact on the PM and SO_2 results (only changed the association between $PM_{2.5}$ and persistent phlegm from positive to positive and significant). However, the new analyses excluding Guangzhou made the associations of NO_x positive with all the six outcomes, although none of the associations reached statistical significance. These results support the within-city positive NO_x associations observed from between- and within-city analyses and suggest that between-city negative associations (and overall negative associations) may be driven by the Guangzhou data pattern.

In summary, the associations found in all types of statistical analyses (overall analyses, within- and between-city analyses, three-cities analyses) should have greater confidences on the findings. The within-city and between-city associations of morbidity prevalence with $PM_{10-2.5}$ were all positive (OR > 1) for all the morbidity outcomes. The analyses for Lanzhou excluded show that $PM_{10-2.5}$ was still positively associated with three morbidity outcomes. Positive within-city and between-city associations of the other PM size fractions were observed with some of the

health outcomes. These results suggest that long-term ambient PM pollution was positively associated with children's respiratory morbidity prevalence in the four Chinese cities and that the associations with coarse particles ($PM_{10-2.5}$) appeared stronger. The early Harvard Six Cities Study found that a number of respiratory morbidity outcomes in schoolchildren (cough or persistent cough, bronchitis, chest illness, wheeze, and/or lower respiratory illness index) were positively associated with ambient particulate (measured as TSP) levels (*16,22*). A more recent Slovakian study has also found that the prevalence of respiratory nonasthmatic symptoms and hospitalizations was associated with increased TSP (*17*).

Besides checking on statistical significances of associations, another way to assess the relative importance in health effects of different air pollutants is to compare the ORs associated with a constant increment in ambient concentration. When scaled to an increment of 50 µg/m³, $PM_{10-2.5}$ had the largest ORs for all the six health outcomes (see Table 7). Interestingly, a time-series study carried out in the Coachella Valley in California provided evidence for a mortality effect of PM_{10} in an area where the particulate mass was dominated by coarse particles (*23*). These findings suggest that the health importance of this fraction of ambient particles should not be underestimated, given that fine particles ($PM_{2.5}$) are gaining more attention nowadays because of their stronger impact on mortality and some morbidity outcomes (*1*). It is clear that certain anthropogenic toxins may be more enriched in fine particles than in coarse particles and that fine particles can penetrate human airways and deposit in the alveolar region, thus leading to cardiopulmonary damage (*1,24*). However, coarse particles may contain chemical and/or biologic agents that can be more relevant to some respiratory morbidity outcomes. The results from several recent studies on the associations between several morbidity outcomes in children (e.g., cough, wheeze, bronchitis, asthma) and PM_{10} or $PM_{2.5}$ were not very consistent (*11–13,25*). Whether coarse particles were better associated with the morbidity outcomes could not be assessed because of the lack of the monitoring data on coarse particles.

Table 5. Associations of air pollutants with respiratory morbidity.

Pollutant (interquartile range)		Wheeze	Asthma	Bronchitis	Hospitalization	Persistent cough	Persistent phlegm
$PM_{2.5}$	OR	1.05	1.22	1.50	1.06	1.18	2.41
(39 µg/m³)	95% CI	0.58–1.92	0.73–2.01	0.55–4.12	0.54–2.07	0.80–1.72	0.85–6.86
$PM_{10-2.5}$	OR	1.12	1.28	2.20*	1.47	1.46*	2.83*
(42 µg/m³)	95% CI	0.65–1.93	0.86–1.91	1.14–4.26	0.86–2.52	1.12–1.90	1.93–4.16
PM_{10}	OR	1.12	1.33	2.09	1.31	1.38	3.21*
(87 µg/m³)	95% CI	0.58–2.15	0.80–2.19	0.81–5.39	0.65–2.67	0.94–2.03	1.55–6.67
TSP	OR	1.28	1.32	2.22*	1.38	1.35*	2.52*
(263 µg/m³)	95% CI	0.83–1.99	0.93–1.86	1.47–3.34	0.86–2.21	1.02–1.79	1.97–3.21
SO_2	OR	1.14	1.03	0.92	0.84	0.99	1.04
(91 µg/m³)	95% CI	0.85–1.53	0.75–1.41	0.40–2.12	0.51–1.39	0.73–1.33	0.38–2.87
NO_x	OR	0.82	0.95	0.90	0.97	1.08	0.99
(64 µg/m³)	95% CI	0.53–1.28	0.63–1.43	0.35–2.29	0.52–1.79	0.77–1.51	0.27–3.66

ORs and 95% CIs were scaled to the interquartile range for each pollutant.
*$p < 0.05$.

Table 6. Between- and within-city modeled ORs, scaled to interquartile range of concentrations for each pollutant.

Condition	$PM_{2.5}$ Between	Within	$PM_{10-2.5}$ Between	Within	PM_{10} Between	Within	TSP Between	Within	SO_2 Between	Within	NO_x Between	Within
Wheeze	0.94	1.06	1.12	1.19	1.04	1.13	1.48	1.11	1.34	1.04	0.50*	1.08
Asthma	1.14	1.27	1.12	1.60	1.17	1.48	1.23	1.69	1.20	1.07	0.77	1.22
Bronchitis	1.58	0.93	3.18*	1.08	2.63	0.98	2.32*	1.00	0.83	1.09	0.73	1.01
Hospitalization	0.94	0.87	1.49	1.07	1.22	0.93	1.30	1.00	0.78	0.94	0.94	0.93
Persistent cough	1.18	1.17	1.42	1.45	1.38	1.33	1.27	1.65	0.95	1.18	0.93	1.17
Persistent phlegm	1.50	1.32	2.78*	1.77	2.38	1.60	2.32*	2.72	0.96	1.35	0.63	1.28

*$p < 0.05$.

Table 7. ORs of morbidity prevalence, associated with a 50 mg/m³ increase in pollutant concentration.

Pollutant	Wheeze	Asthma	Bronchitis	Hospitalization	Persistent cough	Persistent phlegm
$PM_{2.5}$	1.06	1.29	1.68	1.08	1.24	3.09
$PM_{10-2.5}$	1.14	1.34	2.56	1.58	1.57	3.45
PM_{10}	1.07	1.18	1.53	1.17	1.20	1.95
TSP	1.05	1.05	1.16	1.06	1.06	1.19
SO_2	1.07	1.02	0.96	0.91	0.99	1.02
NO_x	0.86	0.96	0.92	0.98	1.06	0.99

Conclusions and Recommendations

As found in many other parts of the world, certain personal, residential, and family factors were associated with prevalence of respiratory morbidities in schoolchildren residing in the eight districts of the Four Chinese Cities Study. Risk factors identified in the present analysis include being younger in the study group, being male (except for persistent cough), having been breast-fed, sharing bedrooms, sharing beds, room being smoky during cooking, eye irritation during cooking, parental smoking, and the history of parental asthma. On the basis of this evidence, reducing cooking smoke and exposures to ETS would clearly be beneficial to children's respiratory health in the Chinese cities. This can be done through some practical steps. For instance, exposure to ETS can be reduced or eliminated when smoking parents quit smoking or smoke outside homes. Exposure to cooking fumes can be reduced by altering cooking methods or making some construction and ventilation modifications to stoves.

The eight study districts exhibited large gradients in ambient concentrations of PM, SO_2, and NO_x; the gradient was as large as up to 532 μg/m³ for TSP (the smallest was still 80 μg/m³ for $PM_{10-2.5}$). The pollutant concentrations were substantially higher in these districts than those in the North American and West European communities of previous studies. However, only the prevalence of bronchitis and the prevalence of persistent cough appeared markedly higher in these Chinese districts. Several types of statistical analyses commonly found positive associations between prevalence of some respiratory morbidity outcomes and outdoor levels of PM with different size fractions. The association

appeared to be stronger for coarse particles ($PM_{10-2.5}$). The results from this study suggest that ambient TSP concentrations can still be an effective index of air pollution in the Chinese cities in relation to children's respiratory symptoms. The results of this study also present some evidence that ambient levels of NO_x and SO_2 were positively associated with children's respiratory symptoms, but the evidence for these two gaseous pollutants appeared to be weaker than that for PM.

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