

**Table 5S-4 Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
<b>United States and Canada</b>			
<p><a href="#">Dockery et al. (1989)</a>            Kingston-Harriman, TN, U.S.; Portage, WI, U.S.; St. Louis, MO, U.S.; Steubenville, OH, U.S.; Topeka, KS, U.S.; Watertown, MA, U.S.            Period of study: 1980–1981 school yr</p>	<p>Cross-sectional assessment of the association between air pollution and chronic respiratory health of 5,422 (10–12 yr) white children examined in the 1980–1981 school yr. Children were part of the cohort of children in the Six Cities Study of Air Pollution and Health. Symptoms were analyzed using logistic regression that included sex, age, indicators of parental education, maternal smoking, indicator for gas stove, and an indicator for city.</p> <p>Respiratory symptoms investigated were bronchitis, chronic cough, chest illness, persistent wheeze, asthma. The logarithm of pulmonary function was fitted to a multiple linear regression model that included sex, sex-specific log of height, age, indicators of parental education, maternal smoking, a gas stove indicator, and city indicator. Annual means of the 24-h avg air pollutant concentration for the 12 mo preceding the examination of each child was calculated for each city.</p>	<p>Daily mean concentrations, averaging hourly concentrations for each day with at least 18 h values</p> <p>Portage: 4.2 ppb            Topeka: 3.5            Watertown: 10.5            Kingston: 6.5            St. Louis: 13.5            Steubenville: 27.8</p>	<p>No significant associations between SO<sub>2</sub> and any pulmonary function measurements. No significant association between SO<sub>2</sub> and symptoms.</p> <p>Relative odds and 95% CI between most/least polluted cities:</p> <p>Bronchitis: 1.5 (0.4, 5.8)            Chronic cough: 1.8 (0.3, 12.5)            Chest illness: 1.5 (0.4, 5.9)            Persistent wheeze: 0.9 (0.4, 1.9)            Asthma: 0.6 (0.3, 1.2)            Reference symptoms:            Hay fever: 0.6 (0.2, 1.7)            Earache: 1.2 (0.3, 5.3)            Nonrespiratory illness: 1.0 (0.6, 1.5)</p> <p>Analysis stratified by asthma or persistent wheeze bronchitis</p> <p>No wheeze or asthma 1.5 (0.5, 4.3)            Yes wheeze or asthma 2.0 (0.3, 14.3)</p> <p>Chronic cough</p> <p>No wheeze or asthma 2.4 (0.5, 11.7)            Yes wheeze or asthma 1.9 (0.1, 44.1)</p> <p>Chest illness</p> <p>No wheeze or asthma 1.5 (0.4, 5.6)            Yes wheeze or asthma 1.9 (0.3, 13.0)</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
<p><a href="#">Dockery et al. (1996)</a> 18 sites in U.S. 6 sites in Canada Period of study: 1988–1991</p>	<p>Study of the respiratory health effects of acid aerosols in 13,369 white children aged 8 to 12 yr old from 24 communities in the U.S. and Canada between 1988 and 1991. Information was gathered by questionnaire and a pulmonary function.</p>	<p>SO<sub>2</sub> avg: Mean: 4.8 ppm SD 3.5 Range 0.2, 12.9</p>	<p>With the exception of the gaseous acids (nitrous and nitric acid), none of the particulate or gaseous pollutants, including SO<sub>2</sub>, were associated with increased asthma or any asthmatic symptoms. Stronger associations with particulate pollutants were observed for bronchitis and bronchitic symptoms.</p> <p>Odds ratio (95% CI) for 12.7 ppb range of SO<sub>2</sub> pollution:</p> <p>Asthma: 1.05 (0.57, 1.93) Attacks of wheeze: 1.07 (0.75, 1.55) Persistent wheeze: 1.19 (0.80, 1.79) Any asthmatic symptoms: 1.16 (0.80, 1.68) Bronchitis: 1.56 (0.95, 2.56) Chronic cough: 1.02 (0.66, 1.58) Chronic phlegm: 1.55 (1.01, 2.37) Any bronchitic symptoms: 1.29 (0.98, 1.71)</p>
<p><a href="#">Euler et al. (1987)</a> California, U.S.</p>	<p>Cross-sectional study of 7,445 (25 yr or older) Seventh-Day Adventists who lived in their 1977 residential areas (Los Angeles and its border counties, San Francisco, and San Diego) for at least 10 yr to determine the effect of long-term cumulative exposure to ambient levels of TSP and SO<sub>2</sub> on COPD symptoms. Study population is subgroup of NCI-funded ASHMOG study that enrolled 36,805 Seventh-Day Adventists in 1974. Each participant's cumulative exposure to the pollutant exceeding four different threshold levels were estimated using monthly</p>	<p>None provided</p>	<p>Study reported that SO<sub>2</sub> exposure was not associated with symptoms of COPD until concentrations exceeded 4 ppm. The correlation coefficient of SO<sub>2</sub> (above 4 ppm) with TSP (above 200 µg/m<sup>3</sup>) the highest exposure levels for these two pollutants was 0.30; thus, the authors believed that it was possible to separate the effects of SO<sub>2</sub> from TSP. Multiple regressions used in the analysis. No significant effect at exposures levels below 4 ppm or above 8 ppm.</p> <p>Relative risk estimate (based on 1,003 cases) SO<sub>2</sub> exposure above 2 ppm during 11 yr of study</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	residence ZIP code histories and interpolated dosages from state monitoring stations. Participants completed a questionnaire on respiratory symptoms, smoking history, occupational history, and residence history.	Continued	2000 h/yr: 1.09 1000 h/yr : 1.04 500 h/yr: 1.03  SO <sub>2</sub> exposure above 4 ppm 500 h/yr : 1.18 250 h/yr: 1.09 100 h/yr: 1.03  SO <sub>2</sub> above 8 ppm 60 h/yr: 1.07 30 h/yr: 1.03 15 h/yr: 1.02  SO <sub>2</sub> above 14 ppm 10 h/yr: 1.03 5 h/yr: 1.01 1 h/yr: 1.00
<a href="#">Goss et al. (2004)</a> United States Period of study: 1999–2000	Cohort study of 18,491 cystic fibrosis patients over 6 yr of age who were enrolled in the Cystic Fibrosis Foundation National Patient Registry in 1999 and 2000. Mean age of patients was 18.4 yr; 92% had pancreatic insufficiency. Air pollution from the Aerometric Information Retrieval System linked with patient's home ZIP code. Air pollutants studied included O <sub>3</sub> , NO <sub>2</sub> , SO <sub>2</sub> , CO, PM <sub>10</sub> , and PM <sub>2.5</sub> . Health endpoints of interest were pulmonary exacerbations, lung function, and mortality. However, study did not have enough power to assess the outcome of mortality. Logistic regression and polytomous regression models that adjusted for sex, age, weight, race, airway colonization, pancreatic function, and insurance status were used.	Mean (SD): 4.91 (2.6) ppb Median: 4.3 ppb IQR: 2.7-5.9 ppb	With the single-pollutant model, no significant association between SO <sub>2</sub> and pulmonary exacerbations. Odds ratio per 10 ppb increase in SO <sub>2</sub> : 0.83 (95% CI: 0.71, 1.01), <i>p</i> = 0.068  No clear association between pulmonary function and SO <sub>2</sub> . No effect estimates provided.
<a href="#">McDonnell et al. (1999)</a> California, U.S. Period of study: 1973–1992	Prospective study (over 15 yr) of 3,091 nonsmokers aged 27-87 yr that evaluated the association between long-term ambient O <sub>3</sub> exposure and the development of adult-onset asthma. Cohort consisted of nonsmoking,	Mean: SO <sub>2</sub> 6.8 µg/m <sup>3</sup> Range: 0.0–10.2 µg/m <sup>3</sup> Spearman correlation coefficient <i>r</i> = 0.25 with O <sub>3</sub>	No significant positive association between SO <sub>2</sub> and asthma for males or females. Addition of a second pollutant to the O <sub>3</sub> model for the male subjects, did not result in a decrease of more than 10% in the magnitude of the

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	<p>non-Hispanic white, California Seventh-Day Adventists who were enrolled in 1977 in the AHSMOG study.</p> <p>Logistic regression used to assess the association between the 1973–1992 mean 8-h avg ambient O<sub>3</sub> concentration and the 1977–1992 incidence of doctor-diagnosed asthma. Levels of PM<sub>10</sub>, NO<sub>2</sub>, and SO<sub>4</sub> were measured but no effect estimates were given.</p>	Continued	<p>regression coefficient for O<sub>3</sub>, and for the females addition did not cause the coefficient for O<sub>3</sub> to become significantly positive.</p>
<p><a href="#">Schwartz (1989)</a> United States Period of study: Feb 1976–Feb 1980</p>	<p>Cross-sectional study using data from the Second National Health and Nutrition Examination Survey (NHANES II) to examine the relation between air pollution and lung function growth in 4,300 children and youths 6–24 yr old. A two-staged analysis was performed that consisted of (1) regression equations including factors known to affect lung function and (2) a regression of the residuals of the first regression on air pollution.</p>	<p>Annual percentiles (ppm): 10th: 0.0060 25th: 0.0106 50th: 0.0131 75th: 0.0159 90th: 0.0193</p>	<p>The study did not find an association between SO<sub>2</sub> and any of the lung function growth measurements (i.e., FVC, FEV<sub>1</sub>, and peak flow).</p>
<b>Europe</b>			
<p><a href="#">Ackermann-Lieblich et al. (1997)</a> Eight communities in Switzerland: (Aarau, Basel, Davos, Geneva, Lugano, Montana, Payerne, and Wald) Period of study: 1991–1993</p>	<p>Cross-sectional population-based study of 9,651 adults (18–60 yr) in eight areas in Switzerland (SAPALDIA), to evaluate the effect of long-term exposure of air pollutants on lung function. Examined the effects of SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>, TSP, and PM<sub>10</sub>. Participants were given a medical exam that included questionnaire data, lung function tests, skin prick testing, and end-expiratory CO concentration. Subjects had to reside in the area for at least 3 yr to be in the study.</p>	<p>Avg SO<sub>2</sub> in 1991 (µg/m<sup>3</sup>): Mean: 11.7 SD: 7.1 Range: 2.5–25.5</p>	<p>Mean values of SO<sub>2</sub>, PM<sub>10</sub>, and NO<sub>2</sub> were significantly associated with reduction in pulmonary function. SO<sub>2</sub> was correlated with PM<sub>30</sub> (<math>r = 0.78</math>), PM<sub>10</sub> (<math>r = 0.93</math>), and NO<sub>2</sub> (<math>r = 0.86</math>). Authors stated that the association with SO<sub>2</sub> disappeared after controlling for PM<sub>10</sub> but no data was shown.</p> <p>Regression coefficients and 95% CI in healthy never smokers (per 10 µg/m<sup>3</sup> increase in annual avg SO<sub>2</sub>) FVC: -0.0325 (-0.0390, -0.0260)</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	Continued	Continued	FEV <sub>1</sub> : -0.0125 (-0.0192, -0.0058)
<p><a href="#">Braun-Fahrlander et al. (1997)</a> 10 communities in Switzerland (Anieres, Bern, Biel, Geneva, Langnau, Lugano, Montana, Payerne, Rheintal, and Zurich) Period of study: 1992-1993</p>	<p>Cross-sectional study of 4,470 children (6-15 yr) living in 10 different communities in Switzerland to determine the effects of long-term exposure to PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> on respiratory and allergic symptoms and illnesses. Part of the Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution (SCARPOL).</p>	<p>Annual avg SO<sub>2</sub> (µg/m<sup>3</sup>): Lugano: 23 Geneva: 13 Zurich: 16 Bern: 11 Anieres: 4 Biel: 15 Rheintal: 8 Langnau: NA Payerne: 3 Montana: 2</p>	<p>This study reported that the annual mean SO<sub>2</sub>, PM<sub>10</sub>, and NO<sub>2</sub> were positively and significantly associated with prevalence rates of chronic cough, nocturnal dry cough, and bronchitis and conjunctivitis symptoms. Strongest association found with PM<sub>10</sub>. However, there was no significant association between SO<sub>2</sub> and asthma or allergic rhinitis. Adjusted relative odds between the most/least polluted community: 2-23 µg/m<sup>2</sup> (0.8, 8.8 ppb) Chronic cough: 1.57 (1.02, 2.42) Nocturnal dry cough: 1.66 (1.16, 2.38) Bronchitis: 1.48 (0.98, 2.24) Wheeze: 0.88 (0.54, 1.44) Asthma (ever): 0.74 (0.45, 1.21) Sneezing during pollen season: 1.07 (0.67, 1.70) Hay fever: 0.84 (0.55, 1.29) Conjunctivitis symptoms: 1.74 (1.22, 2.46) Diarrhea: 1.02 (0.75, 1.39)</p>
<p><a href="#">Charpin et al. (1999)</a> Etang de Berre area of France (Arles, Istres, Port de Bouc, Rognac-Velaux, Salon de Provence, Sausset, and Vitrolles) Period of study: Jan-Feb 1993</p>	<p>Cross-sectional cohort study of 2,073 children (10-11 yr) from seven communities in France (some with the highest photochemical exposures in France) to test the hypothesis that atopy is greater in towns with higher photochemical pollution levels. Mean levels of SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub> were measured for 2 mo in 1993. Children tested for atopy based on skin prick test (house dust mite, cat dander, grass pollen, cypress pollen, and</p>	<p>24-h avg (SD) SO<sub>2</sub> (µg/m<sup>3</sup>): Arles: 29.7 (15.5) Istres: 23.8 (12.7) Port de Bouc: 32.3 (24.5) Rognanc-Velaux: 39.5 (21.8) Salon de Provence: 17.3 (11.6) Sausset: 29.0 (28.7) Vitrolles: 57.4 (32.0)</p>	<p>Study did not demonstrate any association between air pollution and atopic status of the children living in the seven communities, some with high photochemical exposures. A limitation of study is that authors did not consider short-term variation in air pollution and did not have any indoor air pollution measurements.</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	alternaria). To be eligible for the study, subjects must have resided in current town for at least 3 yr. Questionnaire filled out by parents that included questions on SES passive smoking at home. Two-mo mean level of air pollutants used in logistic regression analysis.	Continued	Continued
<a href="#">Frischer et al. (1999)</a> Nine communities in Austria Period of study: 1994–1996	Longitudinal cohort study of 1,150 children (mean age 7.8 yr) to investigate the long-term effects of O <sub>3</sub> on lung growth. Children were followed for 3 yr and lung function was recorded biannually, before and after summertime. The dependent variables were change in FVC, FEV <sub>1</sub> , and MEF <sub>50</sub> . The nine sites were selected to represent a broad range of O <sub>3</sub> exposures. GEE models adjusted for baseline function, atopy, sex, site, environmental tobacco smoke exposure, season, and change in height. Other pollutants studied included PM <sub>10</sub> , SO <sub>2</sub> , and NO <sub>2</sub> .	Annual mean SO <sub>2</sub> (ppb) in 1994: Amstetten: 3.75 St. Valentin: 3.00 Krems: 3.75 Heidenreichstein: 4.13 Ganserndorf: 5.63 Mistelbach: 5.25 Wiesmath: 6.00 Bruck: 4.88 Pollau: 2.25	No consistent association observed between lung function and SO <sub>2</sub> , NO <sub>2</sub> , and PM <sub>10</sub> . A negative effect estimate was observed during the summer and a positive estimate during the winter.  Change in lung function (per ppb SO <sub>2</sub> ): FEV <sub>1</sub> (mL/day): Summer: -0.018 (0.004), <i>p</i> < 0.001 Winter: 0.003 (0.001), <i>p</i> < 0.001 FVC (mL/day): Summer: -0.009 (0.004), <i>p</i> = 0.02 Winter: 0.002 (0.001), <i>p</i> = 0.03 MEF <sub>50</sub> (mL/s/day): Summer: -0.059 (0.010), <i>p</i> < 0.001 Winter: 0.003 (0.003), <i>p</i> = 0.26
<a href="#">Frischer et al. (2001)</a> Nine communities in Austria Period of study: Sep–Oct 1997	Cross-sectional cohort study of 877 children (mean age 11.2 yr) living in nine sites with different O <sub>3</sub> exposures. Urinary eosinophil protein (U-EPX) measured as a marker of eosinophil activation. U-EPX determined from a single spot urine sample analyzed with linear regression models.	30-min avg SO <sub>2</sub> : 30-day mean 2.70 ppb IQR 2.1 ppb	No significant association between SO <sub>2</sub> and U-EPX. Regression coefficient and SE: -10.57 (0.25) per ppb SO <sub>2</sub>

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Study	Methods	Pollutant Data	Findings
<p><a href="#">Frye et al. (2003)</a> Zerbst, Hettstedt, Bitterfeld, East Germany Period of study: 1992–93, 1995–1996, 1998–1999</p>	<p>Three consecutive cross-sectional surveys of children (11-14 yr) from three communities in East Germany. Parents of 3,155 children completed a questionnaire on symptoms. Lung function tests performed on 2,493 children. Study excluded children if they lived for less than 2 yr in current home and if their previous home was more than 2 km away. The log-transformed lung function parameters were used as the response variables in a linear regression analysis that controlled for sex, height, season of examination, lung function equipment, parental education, parental atopy, and environmental tobacco smoke. Used avg of annual means of pollutants 2 yr preceding each survey.</p>	<p>Used avg of annual means of pollutants 2 yr preceding health measurement High of 113 µg/m<sup>3</sup> (in Bitterfeld) to a low of 6 µg/m<sup>3</sup>. (Pollution values only described in figure)</p>	<p>The annual mean TSP declined from 79 to 25 µg/m<sup>3</sup> and SO<sub>2</sub> from 113 to 6 µg/m<sup>3</sup> and the mean FVC and FEV<sub>1</sub> increased from 1992–1993 to 1998–1999. Study concluded that reduction of air pollution in a short time period may improve children's lung function. Percent change of lung function for a 100-µg/m<sup>3</sup> decrease in SO<sub>2</sub> 2 yr before the investigation (N = 1,911) FVC: 4.9 (0.7, 9.3) FEV<sub>1</sub>: 3.0 (-1.1, 7.2) FEV<sub>1</sub>/FVC: -1.5 (-3.0, 0.1)</p>
<p><a href="#">Garcia-Marcos et al. (1999)</a> Cartagena, Spain Period of study: winter 1992</p>	<p>A total of 340 children (10–11 yr) living in and attending schools within a polluted and a relatively nonpolluted area were included in this study which aimed to establish the relative contribution socioeconomic status, parental smoking, and air pollution have on asthma symptoms, spirometry, and bronchodilator response. Parents completed questionnaire on respiratory symptoms and risk factors including, living in polluted area, maternal smoking, paternal smoking, number of people living in the house, proximity to heavy traffic roads. Spirometry was performed before and after an inhaled 0.2 mg fenoterol was delivered to determine bronchodilator response. Bronchodilator response was considered positive if</p>	<p>Annual mean SO<sub>2</sub> (µg/m<sup>3</sup>): Polluted areas: 75 µg/m<sup>3</sup> Nonpolluted areas: 20 µg/m<sup>3</sup></p>	<p>This study found that living in the polluted areas reduced the risk of a positive bronchodilator response (RR = 0.61, p = 004).</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

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Continued	the FVC after fenoterol was increased by at least 10% or PEF by 12%. Logistic regression included as independent variables all the risk factors.	Continued	Continued
<a href="#">Gokirmak et al. (2003)</a> Malatya, Turkey	Study on occupational exposure to SO <sub>2</sub> in apricot sulfurization workers that investigated the role of oxidative stress resulting in exposure to high concentrations of SO <sub>2</sub> on bronchoconstriction. Forty workers (mean age 28 yr, range 16–60 yr) who have been working in apricot sulfurization for 20–25 days each yr and 20 controls (mean age 29 yr, range 17–42) who had no SO <sub>2</sub> exposure participated in the study. Activities of antioxidant enzymes [glutathione peroxidase (GSHPx), superoxide dismutase (SOD), and catalase], malondialdehyde (MDA) concentrations (marker of lipid peroxidation), and pulmonary function test measured in subjects.	SO <sub>2</sub> conc ranged from 106.6 to 639.2 ppm in nine apricot farms. Mean conc around sulfurization chamber: 324.1 (35.1) ppm	SOD, GSH-Px, and catalase activities were lower and malondialdehyde concentrations were higher in the apricot sulfurization workers compared to controls. Pulmonary function decreased after SO <sub>2</sub> exposure among the apricot sulfurization workers. Authors concluded that occupational exposure to high concentrations of SO <sub>2</sub> enhances oxidative stress and that lipid peroxidation may be a mechanism of SO <sub>2</sub> induced bronchoconstriction. Apricot sulfurization workers vs. controls Mean (SD) SOD (U/mL): 2.2 (0.6) vs. 3.2 (0.7) U/mL, <i>p</i> < 0.0001 Glutathione peroxidase (U/mL): 0.6 (0.3) vs. 1.1 (0.3), <i>p</i> < 0.0001 Catalase (L/L): 107.6 (27.4) vs. 152.6 (14.3), <i>p</i> < 0.0001 MDA (nmol/L): 4.1 (0.9) vs. 1.9 (5.3), <i>p</i> < 0.0001 Before vs. after SO <sub>2</sub> exposure among apricot sulfurization workers Mean (SD) FVC (% predicted) 88 (17) vs. 84 (16), <i>p</i> < 0.001 FEV <sub>1</sub> (% predicted) 98 (14) vs. 87 (14), <i>p</i> < 0.001 FEV <sub>1</sub> /FVC: 92 (7) vs. 86 (9), <i>p</i> < 0.001

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	Continued	Continued	FEF <sub>25-75%</sub> (% predicted) 108 (19) vs. 87 (23), <i>p</i> < 0.001
<a href="#">Heinrich et al. (2002)</a> Reunified Germany (Bitterfeld, Hettstedt, and Zerbst) Period of study: 1992–1993, 1995–1996, 1998–1999	Three cross-sectional surveys of children (5–14 yr) from three areas that were formerly part of East Germany to investigate the impact of declines in TSP and SO <sub>2</sub> on prevalence of nonallergic respiratory disorders in children. Study excluded children if they lived for less than 2 yr in current home and if their previous home was more than 2 km away. GEE used for analysis.	SO <sub>2</sub> concentration in µg/m <sup>3</sup> Yr/Zerbst/Bitterf/Hettst: 1991/78/113/84 1992/58/75/46 1993/42/60/49 1994/29/35/38 1995/21/30/26 1996/25/24/25 1997/13/13/13 1998/8/9/6	Study found that SO <sub>2</sub> exposure was significantly associated with prevalence of bronchitis, frequent colds, and febrile infections. While results are reported as risk for an increase in air pollutant, the respiratory health of children improved with declines in TSP and SO <sub>2</sub> . Authors concluded that exposure to combustion-derived air pollution is causally related to nonallergic respiratory health in children.  Odds ratio and 95% CI (per 100 µg/m <sup>3</sup> in 2 yr mean SO <sub>2</sub> ): All children: Bronchitis: 2.72 (1.74, 4.23) Otitis media: 1.42 (0.94, 2.15) Sinusitis: 2.26 (0.85, 6.04) Frequent colds: 1.81 (1.23, 2.68) Febrile infections: 1.76 (1.02, 3.03) Cough in morning: 1.10 (0.73, 1.64) Shortness of breath: 1.31 (0.84, 2.03)  Children without indoor exposures (living in damp houses with visible molds, ETS in the home, gas cooking emissions, and contact with cats): Bronchitis: 4.26 (2.15, 8.46) Otitis media: 1.43 (0.73, 2.81) Sinusitis: 2.95 (0.52, 16.6) Frequent colds: 2.29 (1.15, 4.54) Febrile infections: 1.75 (0.78, 3.91) Cough in morning: 1.00 (0.38, 2.64) Shortness of breath: 2.07 (0.90, 4.75)

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
<a href="#">Herbarth et al. (2001)</a> East Germany Period of study: 1993–1997	Meta-analysis of three cross-sectional studies: (1) Study on Airway Diseases and Allergies among Kindergarten Children (KIGA); (2) the Leipzig Infection, Airway Disease, and Allergy Study on School Starters (LISS); and (3) KIGA-IND, which was based on the KIGA design but conducted in three differentially polluted industrial areas. A total of 3,816 children participated in the three studies. Analysis of data from parent-completed questionnaires to determine the effect of lifetime exposure to SO <sub>2</sub> and TSP on the occurrence of acute bronchitis. Total lifetime exposure burden corresponds to the exposure duration from birth to time of the study. The LISS study was divided in to LISS-U for the urban area and LISS-R for the rural area. Logistic regression analysis used that adjusted for predisposition in the family (mother or father with bronchitis), ETS, smoking during pregnancy or in the presence of the pregnant women.	Avg lifetime exposure burden of SO <sub>2</sub> (µg/m <sup>3</sup> ): KIGA: 142 LISS: 48 LISS: R 47 KIGA-IND: 59	This study found the highest bronchitis prevalence in the KIGA cohort and the lowest in the LISS cohort, which is consistent with the SO <sub>2</sub> concentrations in these cohorts. Study found a correlative link between SO <sub>2</sub> and bronchitis ( $R = 0.96, p < 0.001$ ) but not TSP ( $R = 0.59$ ). Results of study suggest that SO <sub>2</sub> may be a more important factor than TSP in the occurrence of bronchitis in these study areas. Odds ratio for bronchitis adjusted for parental predisposition, smoking, and lifetime exposure to SO <sub>2</sub> and TSP (two-pollutant model). SO <sub>2</sub> : 3.51 (2.56, 4.82) TSP: 0.72 (0.49, 1.04)
<a href="#">Hirsch et al. (1999)</a> Dresden, Germany	Cross-sectional study to relate the prevalence of respiratory and allergic diseases in childhood to measurements of outdoor air pollutants. 5,421 children ages 5–7 yr and 9–11 yr were evaluated by questionnaires, skin-prick testing, venipuncture for (Ig)E, lung function, and bronchial challenge test.	Mean (µg/m <sup>3</sup> ): 48.3 Range: 29.0–69.3 25–75 percentile 42.7–54.3	SO <sub>x</sub> was positively associated with current morning cough but not with bronchitis. Prevalence odds ratio (95% CI) for symptoms within the past 12 mo, +10 µg/m <sup>3</sup> : Wheeze: Atopic 1.03 (0.79, 1.35) µg/m <sup>3</sup> ; Nonatopic 1.36 (1.01, 1.84) Morning cough: Atopic 1.22 (0.92, 1.61)

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	Continued	Continued	Nonatopic 1.32 (1.07, 1.63) Prevalence odds ratio (95% CI) for doctor's diagnosis, +10 µg/m <sup>3</sup> : Asthma: Atopic 1.07 (0.79, 1.45) Nonatopic 1.35 (1.00, 1.82) Bronchitis: Atopic 1.04 (0.87, 1.25) Nonatopic 0.99 (0.88, 1.12)
<a href="#">Horak et al. (2002)</a> Eight communities in Austria Period of study: 1994–1997	Longitudinal cohort study that continued the work of <a href="#">Frischer et al. (1999)</a> by adding 1 more yr of data and analyzing the effects of PM <sub>10</sub> in addition to SO <sub>2</sub> , NO <sub>2</sub> , and O <sub>3</sub> . At the beginning of the study 975 children (mean age 8.11 yr) were recruited for the study, but only 80.6% of the children performed all six lung function tests (twice a yr). The difference for each lung function parameter between two subsequent measures was divided by the days between measurements and presents as difference per day (dpd) for that parameter. 860 children were included in the GEE analysis that controlled for sex, atopy, passive smoking, initial height, height difference, site, and initial lung function.	Seasonal avg SO <sub>2</sub> µg/m <sup>3</sup> : Winter: Mean: 16.8 Range: 7.5, 37.4 Summer: Mean : 6.9 µg/m <sup>3</sup> Range: 3.1, 11.7	Moderate correlation between PM <sub>10</sub> and SO <sub>2</sub> in the winter ( $r = 0.52$ ). In a one-pollutant model for SO <sub>2</sub> , long-term seasonal mean concentration of SO <sub>2</sub> had a positive association with FVC dpd and FEV <sub>1</sub> dpd in the winter, but no effect on MEF <sub>25-75</sub> dpd. In a two-pollutant model with PM <sub>10</sub> , wintertime SO <sub>2</sub> had a positive association with FEV <sub>1</sub> dpd.  Single-pollutant model FVC dpd: Summer: 0.009, $p = .336$ ; Winter: 0.006, $p = .009$ FEV <sub>1</sub> dpd: Summer: 0.005, $p = 0.576$ ; Winter: 0.005, $p = 0.013$ MEF <sub>25-75</sub> : Summer: 0.015, $p = 0.483$ ; Winter: 0.003, $p = 0.637$  Two-pollutant model: SO <sub>2</sub> + PM <sub>10</sub> FVC dpd: Summer: 0.008, $p = 0.395$ ; Winter: 0.004, $p = 0.225$ FEV <sub>1</sub> dpd: Summer: 0.010 (0.271); Winter: 0.007 (0.025) MEF <sub>25-75</sub> dpd: Summer: 0.037, $p = 0.086$ ; Winter: 0.007, $p = 0.429$
<a href="#">Jedrychowski (1999)</a> Krakow, Poland	Cohort prospective study consisting of 1,001 preadolescent children (9 yr old) from two areas of Krakow, Poland.	Annual avg: City center (µg/m <sup>3</sup> ): 43.87 (32.69)	The study did not provide individual estimates for SO <sub>2</sub> .

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Period of study: 1995 (Mar–Jun) and 1997 (Mar–Jun)	The study examined lung function growth using FVC and FEV <sub>1</sub> measurements taken in 1995 and then again 2 yr later, 1997. Used a two-stage analysis that consisted of (1) multivariate linear regression analyses to determine body variables that are significant predictors of lung function growth, and then (2) multivariate logistic regression to examine the relation between air pollution and lung function growth.	Control area (µg/m <sup>3</sup> ): 31.77 (21.93)	Continued
<a href="#">Koksal et al. (2003)</a> Malatya, Turkey	Study on occupational exposure to high concentrations of SO <sub>2</sub> on respiratory symptoms and pulmonary function on apricot sulfurization workers. Apricot sulfurization workers (N = 69) from 15 apricot farms who have been working in sulfurization of apricots for 20–25 days a yr during each summer were recruited for the study.  Subjects rated symptoms (itchy eyes, runny nose, stuffy nose, itchy or scratchy throat, cough, shortness of breath, phlegm, chest pain, and fever) before, during, and 1 h after each exposure.	SO <sub>2</sub> conc ranged from 106.6 to 721.0 ppm	SO <sub>2</sub> exposure at high concentrations increased symptoms of itchy eyes, shortness of breath, cough, running and/or stuffy nose, and itchy or scratchy throat during exposure ( <i>p</i> < 0.05). Inhalation of high concentrations of SO <sub>2</sub> for 1 h caused significant decreases in pulmonary function. Difference in pulmonary function measured before and after exposure: FVC (L) 0.16 (0.42), <i>p</i> < 0.05 FEV <sub>1</sub> (L) 0.39 (0.36), <i>p</i> < 0.001 FEV <sub>1</sub> /FVC: 5.22 (6.75), <i>p</i> < 0.001 PEF (L/s) 1.39 (1.06), <i>p</i> < 0.001 FEF <sub>25–75%</sub> (L/s) 0.82 (0.70), <i>p</i> < 0.001
<a href="#">Kopp et al. (2000)</a> Ten communities in Austria and SW Germany	Longitudinal cohort study of 797 children (mean age 8.2 yr) from 2nd and 3rd grades of 10 schools in Austria and SW Germany to assess the effects of ambient O <sub>3</sub> on lung function in children over a two-summer period. Study also examined the association between avg	Mean SO <sub>2</sub> (95% CI) ppb: Apr–Sep 1994 Amstetten: 3.7 (0.7, 3.9) St Valentin: 2.6 (1.5, 5.2) Krems: 3.7 (0.7, 7.5) Villingen: 0.7 (0, 3.0) Heidenreichstein: 3.7, (0.7, 7.5) Ganserndorf: 3.7 (0.7, 11.2) Mistelbach: 3.7 (0.7, 7.5) Wiesmath: 6.3 (3.4, 9.4)	Lower FVC and FEV <sub>1</sub> increases observed in children exposed to high ambient O <sub>3</sub> levels vs. those exposed to lower levels in the summer. This study found no effect of SO <sub>2</sub> and PM <sub>10</sub> on FVC increase during the summer of 1995 and winter 1994/1995; however, SO <sub>2</sub> was negatively associated with

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	daily lung growth and SO <sub>2</sub> , NO <sub>2</sub> , and PM <sub>10</sub> . Each child performed four lung function tests during spring 1994 and summer 1995. ISAAC questionnaire used for respiratory history. Linear regression models used to assess effect of air pollutants on FVC and FEV <sub>1</sub> , which were surrogates of lung growth	<p>Bruck: 1.5 (0.7, 4.1)            Freudenstadt: 0.7 (0, 3.0)            Oct 1994–Mar 1995            Amstetten: 3.7 (0.7, 7.5)            St Valentin: 3.0 (1.1, 9.4)            Krems: 3.7 (0.7, 11.0)            Villingen: 1.9 (0, 3.0)            Heidenreichstein: 3.7 (0.7, 15.0)            Ganserndorf: 3.7 (0.7, 22.5)            Mistelbach: 3.7 (0.7, 22.5)            Wiesmath: 2.23 (0.7, 10.1)            Bruck: 15 (1.1, 7.9)            Freudenstadt: 1.57 (0.4, 5.3)            Apr–Sep 1995            Amstetten: 3.7 (0.7, 3.8)            St Valentin: 2.6 (1.1, 6.8)            Krems: 3.7 (0.5, 3.8)            Villingen: 0.7 (0, 2.6)            Heidenreichstein: 0.7 (0.5, 0.9)            Ganserndorf: 3.7 (0.7, 7.5)            Mistelbach: 3.7 (0.7, 7.5)            Wiesmath: 7.5 (0.7, 14.9)            Bruck: 3.7 (0.4, 4.9)            Freudenstadt: 0.7 (0, 3.4)</p>	<p>FVC during the summer of 1994.            Change in FVC (per ppb SO<sub>2</sub>)            Summer 1994: -0.044, <i>p</i> = 0.006            Winter 1994/95: 0.007, <i>p</i> = 0.243            Summer 1995: 0.045, <i>p</i> = 0.028</p>
<a href="#">Kramer et al. (1999)</a> East and West Germany Period of study: 1991–1995	<p>Repeated cross-sectional studies between 1991 and 1995 on 7-yr-old children in East Germany and between 1991 and 1994 in West Germany. Comparison of prevalence of airway diseases and allergies in East and West Germany during the first 5 yr after reunification. A total of 19,090 children participated in the study. Logistic regression used to assess the effect of SO<sub>2</sub> and TSP on airway diseases and allergies. Analysis performed on 14,144 children with information on all covariates of interest.</p>	<p>East Germany 2-yr avg concentration ranged from 45–240 µg/m<sup>3</sup>.            West Germany 2-yr avg concentration ranged from 18–33.</p>	<p>All infectious airway diseases and irritation of the airway was associated with either SO<sub>2</sub> or TSP in East Germany in 1991. The decrease of pollution between 1991 and 1995 had a favorable effect on the prevalence of these illnesses. SO<sub>2</sub> was significantly associated with more than five colds in the last 12 mo, tonsillitis, dry cough in the last 12 mo, and frequent cough in 1991–1995.            Odds ratio and 95% CI (per 200 µg/m<sup>3</sup> SO<sub>2</sub>) in East Germany areas, 1991–1995 for children living at least 2 yr in the areas, adjusted for time trend:            Infectious airway diseases:            Pneumonia ever diagnosed: 1.17 (0.85, 1.62)</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	Continued	Continued	Bronchitis, ever diagnosed: 0.85 (0.68, 1.05) ≥5 colds in last 12 mo: 1.55 (1.18, 2.04) Tonsillitis in the last 12 mo: 1.89 (1.49, 2.39) Dry cough in the last 12 mo: 1.46 (1.12, 1.91) Frequent cough ever: 2.51 (1.79, 3.53) Allergic diseases and symptoms: Irritated eyes in the last 12 mo: 1.06 (0.66, 1.70) Irritated nose in the last 12 mo: 1.26 (0.96, 1.66) Wheezing ever diagnosed: 0.68 (0.46, 1.01) Bronchial asthma ever diagnosed: 2.73 (1.24, 6.04) Hay fever ever diagnosed: 0.60 (0.24, 1.52) Eczema ever diagnosed: 0.87 (0.65, 1.18) Allergy ever diagnosed: 0.93 (0.67, 1.29)
<a href="#">Liebhart et al. (2007)</a> Bialystok, Bydgoszcz, Gdansk, Krakow, Lublin, Lodz, Poznan, Rabka, Warszawa, Wroclaw, and Zabrze, Poland Period of study: 1998–1999	The Polish Multicentre Study of Epidemiology of Allergic Diseases (PMSEAD), which consisted of a cohort of 16,238 individuals aged 3–80 yr old from 33 areas in 11 regions of Poland. Asthma diagnosis was determined through household questionnaires. Conducted multivariate and univariate logistic regression analyses to examine the prevalence of and risk factors for asthma.	Range (µg/m <sup>3</sup> ): 4.0–35.0	In multivariate logistic regression models, BS was found to be a significant risk factor for asthma for both children and adults. SO <sub>2</sub> was found to be a significant risk factor for asthma in both children and adults, but only in a univariate logistic regression. Adjusted odds ratio (95% CI): Univariate logistic regression Children: 1.34 (1.04, 1.72) Adults: 1.19 (1.02, 1.38) Multivariate logistic regression Children: 1.20 (0.91, 1.59) Adults: 1.01 (0.85, 1.20)

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
<a href="#">Kohlhammer et al. (2007)</a> Hettstedt, Germany Period of study: 1992–1999	Three repeated cross-sectional studies of 5,360 children ages 5–14 yr examining health impacts (lifetime pneumonia) of social and environmental factors.	---	No relationship between SO <sub>2</sub> and pneumonia was observed.
<a href="#">Penard-Morand et al. (2006)</a> Six communities in France (Bordeaux, Clermont-Ferrand, Creteil, Marseille, Strasbourg, and Reims) Period of study: Mar 1999–Oct 2000	Cross-sectional study of 4,901 children (9–11 yr) from 108 randomly selected schools in six cities to assess the association between long-term exposure to background air pollution (NO <sub>2</sub> , SO <sub>2</sub> , PM <sub>10</sub> , O <sub>3</sub> ) and atopy and respiratory outcomes. Analysis restricted to children who had lived at least the last 3 yr in their house at the time of the examination. Analysis used 3-yr avg air pollutant concentrations at the children’s schools. Parents completed questionnaire on respiratory and allergic disorders [asthma, allergic rhinitis (AR), and atopic dermatitis] and children underwent examination that included a skin prick test to assess allergic sensitization, evidence of visible flexural dermatitis, and measure of exercise-induced bronchial reactivity (EIB).	Estimated 3-yr avg concentrations at 108 schools Low concentration: 4.6 µg/m <sup>3</sup> (range: 1.3, 7.4), High conc: 9.6 µg/m <sup>3</sup> (range 7.7, 13.7)	Increased concentrations of SO <sub>2</sub> were significantly associated with an increased risk of EIB, lifetime asthma, and lifetime AR. Pastyr wheeze and asthma were also associated with SO <sub>2</sub> . In a two-pollutant model with PM <sub>10</sub> , significant associations were observed between SO <sub>2</sub> and EIB and pastyr wheeze. Odds ratio and 95% CI (per 5 µg/m <sup>3</sup> SO <sub>2</sub> ): EIB: 1.39 (1.15, 1.66), <i>p</i> < 0.001 Flexural dermatitis: 0.86 (0.73, 1.02), <i>p</i> < 0.10 Pastyr wheeze: 1.23 (1.0, 1.51), <i>p</i> < 0.05 Pastyr asthma: 1.28 (1.00, 1.65), <i>p</i> < 0.01 Pastyr rhinoconjunctivitis: 1.05 (0.89, 1.24) Pastyr atopic dermatitis: 1.01 (0.86, 1.18) Lifetime asthma: 1.19 (1.00, 1.41), <i>p</i> < 0.10 Lifetime allergic rhinitis: 1.16 (1.01, 1.32), <i>p</i> < 0.05 Lifetime atopic dermatitis: 0.93 (0.82, 1.05) Two-pollutant model with PM <sub>10</sub> EIB: 1.46 (1.12, 1.90) Pastyr wheeze: 1.45 (1.09, 1.93)

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
<p><a href="#">Pikhart et al. (2001)</a> Czech Republic, Poland Period of study: 1993–1994</p>	<p>Part of the Small-Area Variation in Air Pollution and Health (SAVIAH) study to assess long-term effects of air pollution on respiratory outcomes. Analysis on data from two centers of the multicenter study: Prague, Czech Republic and Poznan, Poland. Both cities had wide variation in air pollution levels. Parents/guardians of 6,959 children (7–10 yr) completed a questionnaire about the socioeconomic situation of the family, type of housing, family history of atopy, parental smoking, family composition, and health of the child. SO<sub>2</sub> was measured at 80 sites in Poznan and 50 sites in Prague during 2-week campaigns. From these data, GIS was used to estimate pollutant concentrations at a small area level. Logistic regression used to assess effect of air pollution on the prevalence of respiratory outcomes.</p>	<p>Mean SO<sub>2</sub> (µg/m<sup>3</sup>): Prague: 83.9 (range: 65.8–96.6) Poznan: 79.7 (range: 44.2–140.2)</p>	<p>SO<sub>2</sub> levels (mean of home and school) were associated with the prevalence of wheezing/whistling in the past 12 mo. There was a marginal association between SO<sub>2</sub> and lifetime prevalence of wheezing and physician diagnosed asthma. Fully adjusted model controlled for age, sex, maternal education, number of siblings, dampness at home, heating and cooking on gas, maternal smoking, and family history of atopy and center. Authors noted SO<sub>2</sub> is strongly spatially correlated with particles in the Czech Republic and probably Poland, so SO<sub>2</sub> may be proxy for exposure to other pollutants. No other pollutants measured in study.</p> <p>Odds ratio (per 50 µg/m<sup>3</sup>) SO<sub>2</sub>:</p> <p>Wheezing/whistling in past 12 mo: 1.32 (1.10, 1.57) Wheezing/whistling ever: 1.13 (0.99, 1.30) Asthma ever diagnosed by doctor: 1.39 (1.01, 1.92) Dry cough at night: 1.06 (0.89, 1.27)</p>
<p><a href="#">Ramadour et al. (2000)</a> Seven towns in SE France Period of study: Jan–Feb 1993</p>	<p>Cross-sectional cohort study of 2,445 children (age 13–14 yr) who had lived for at least 3 yr in their current residence to compare the levels of O<sub>3</sub>, SO<sub>2</sub>, and NO<sub>2</sub> to the prevalence rates of rhinitis, asthma, and asthmatic symptoms. Some of the communities had the heaviest photochemical exposure in France. Subjects completed ISAAC survey of asthma and respiratory symptoms. Analysis conducted with logistic regression models that controlled for family</p>	<p>Mean (SD) µg/m<sup>3</sup> of SO<sub>2</sub> during 2-mo period: Port de Bouc: 32.3 (24.5) Istres: 23.8 (12.7) Sausset: 29.0 (28.7) Rognanc-Veloux: 39.5 (21.8) Vitrolles: 57.4 (32.0) Arles: 29.7 (15.5) Salon: 17.3 (11.6)</p>	<p>Study found no relationship between mean levels of SO<sub>2</sub>, NO<sub>3</sub>, or O<sub>3</sub> and rhinitis ever, 12-mo rhinitis, rhinoconjunctivitis, and hay fever or asthmatic symptoms. Simple regression analyses of respiratory outcomes vs. mean SO<sub>2</sub> levels in the seven towns indicated that nocturnal dry cough was associated with mean SO<sub>2</sub> levels (<i>r</i> = 0.891). Potential confounding across towns.</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	history of asthma, personal history of early-life respiratory diseases, and SES. Also performed simple univariate linear regressions.	Continued	Continued
<a href="#">Soyseth et al. (1995)</a> Ardal and Laerdal, Norway Period of study: winter seasons 1989–92	Cross-sectional study of 529 children (aged 7–13 yr) to determine whether exposure to SO <sub>2</sub> during infancy is related to the prevalence of bronchial hyperresponsiveness (BHR). A SO <sub>2</sub> emitting aluminum smelter is present in Ardal, but there is no air-polluting industry in Laerdal. Parents filled out a questionnaire regarding family history of asthma, type of housing, respiratory symptoms and parent's smoking habits. Spirometry was performed on each child and bronchial hyperactivity was determined by methacholine challenge or reversibility test. Skin prick test was done to assess atopy. The effects of fluoride were also examined.	Median SO <sub>2</sub> : 37.1 µg/m <sup>3</sup> at ages 0–12 mo 37.9 µg/m <sup>3</sup> at ages 13–36 mo	This study found that the risk of BHR was associated with SO <sub>2</sub> exposure at 0–12 mo Odds ratio for BHR (per 10 µg/m <sup>3</sup> SO <sub>2</sub> ) for various ages at exposure 0–12 mo: 1.62 (1.11, 2.35) 13–36 mo: 1.40 (0.90, 2.21) 37–72 mo: 1.19 (0.77, 1.82) 73–108 mo: 1.19 (0.63, 2.22)
<a href="#">Studnicka et al. (1997)</a> Austria (eight nonurban communities) Period of study: 1991–1993	Longitudinal study of 843 children 7 yr old from eight nonurban Austrian communities. A logistic regression was used to examine the association between SO <sub>2</sub> concentrations and asthma and respiratory symptoms by comparing low, regular, and high SO <sub>2</sub> communities with very low SO <sub>2</sub> communities.	Range: Jan 1991–Dec 1993 (ppb): 6.0 (Krems), 12.0 (Mistel. and Gäns)	SO <sub>2</sub> was significantly associated with bronchial asthma in the last 12 mo and positively associated with parent-reported “ever asthma” when comparing low SO <sub>2</sub> concentration communities with very low SO <sub>2</sub> communities. Adjusted prevalence odds ratio Wheeze last 12 mo: Low: 0.68, regular: 0.88, high: 0.42 Cough apart from colds last 12 mo: Low: 0.75, regular: 0.85, high: 0.72 Bronchitis last 12 mo:

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	Continued	Continued	Low: 0.21, regular: 0.45, high: 0.56 Bronchial asthma last 12 mo: Low: 2.35, regular: 0.22, high: 0.33 Parent-reported "ever asthma": Low: 1.70, regular: 0.23, high: 0.67
<a href="#">Von Mutius et al. (1995)</a> Leipzig, East Germany Period of study: Oct 1991–Jul 1992	The effects of high to moderate levels of air pollution (SO <sub>2</sub> , NO <sub>x</sub> , and PM) on the incidence of upper respiratory were investigated in 1,500 school children (9-11 yr) in Leipzig, East Germany. Logistic regression models controlled for paternal education, passive smoke exposure, number of siblings, temperature, and humidity.	During winter mo, SO <sub>2</sub> daily max concentrations ranged from 40–1283 µg/m <sup>3</sup> . During high pollution period, avg concentration of SO <sub>2</sub> was 188 µg/m <sup>3</sup> and during low pollution avg was 57 µg/m <sup>3</sup> .	The daily mean values of SO <sub>2</sub> and NO <sub>x</sub> were significantly associated with increased risk of developing upper respiratory illnesses during the high concentration period. In the low concentration period, only NO <sub>x</sub> daily mean values were associated with increased risks. In a two-pollutant model with PM, similar estimates to the single-pollutant model were obtained; thus, collinearity of data may not account for the effects of high mean concentrations of SO <sub>2</sub> . Odds ratio and 95% CI (did not indicate per what level of SO <sub>2</sub> increase): Daily mean SO <sub>2</sub> : High period: 1.72 (1.19, 2.49); Low period: 1.40 (0.95, 2.07) Daily max SO <sub>2</sub> : High period: 1.26 (0.80, 1.96); Low period: 0.99 (0.66, 1.47)
<b>Latin America</b>			
<a href="#">Sole et al. (2007)</a> São Paulo, Brazil [São Paulo West (SPW), São Paulo South (SPS), Santo André (SA), Curitiba (CR), Porto Alegre (PoA)]	Cohort of 16,209 adolescents (13–14 yr old) from the 21 centers involved in the International Study of Asthma and Allergies in Childhood (ISAAC). Each	NR	In the analysis of the risk of allergy-related symptoms due to SO <sub>2</sub> levels in relation to the center with the lowest annual mean SO <sub>2</sub> concentrations, SPW was significantly associated with

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	<p>participant was given a questionnaire to identify various allergy-related symptoms that occurred in the last 12 mo. The relationship between affirmative answer to a question, socioeconomic status, and air pollutants was analyzed by the Spearman correlation coefficient. The location with the lowest level of a specific air pollutant was defined as the reference and the risk of an affirmative answer to a question was presented as an odds ratio for each location.</p>	Continued	<p>every symptom. Other significant associations were observed in SA for current wheezing; in CR for rhinitis and rhinoconjunctivitis; and in PoA for current wheezing, nighttime cough, rhinitis, and eczema.</p> <p>Odds ratio (95% CI)Reference center: São Paulo South (SPS):</p> <p>Current wheezing:            SPW: 1.21 (1.08, 1.38);            SA: 1.31 (1.16, 1.48);            CR: 1.02 (0.90, 1.15)            PoA: 1.68 (0.85, 1.10)</p> <p>Severe asthma:            SPW: 2.01 (1.56, 2.60);            SA: 1.04 (0.78, 1.40);            CR: 1.08 (0.81, 1.42);            PoA: 1.01 (1.29, 2.20)</p> <p>Nighttime cough:            SPW: 1.14 (1.03, 1.26);            SA: 0.94 (0.85, 1.04);            CR: 0.93 (0.84, 1.02);            PoA: 1.25 (0.91, 1.12)</p> <p>Rhinitis last yr:            SPW: 1.14 (1.02, 1.27);            SA: 1.05 (0.94, 1.18);            CR: 1.71 (1.54, 1.90);            PoA: 1.36 (1.12, 1.40)</p> <p>Rhinoconjunctivitis:            SPW: 1.78 (1.55, 2.04);            SA: 1.15 (0.99, 1.33);            CR: 1.50 (1.31, 1.72);            PoA: 1.48 (1.18, 1.57)</p> <p>Severe Rhinitis:            SPW: 1.50 (1.32, 1.71);            SA: 1.08 (0.94, 1.24);            CR: 1.52 (1.34, 1.73);            PoA: 0.97 (1.30, 1.69)</p> <p>Eczema:            SPW: 1.40 (1.17, 1.68); SA: 1.00 (0.83, 1.21);            CR: 0.88 (0.72, 1.06);            PoA: 1.40 (0.80, 1.18)</p> <p>Flexural eczema:            SPW: 2.00 (1.58, 2.52);            SA: 0.95 (0.73, 1.24);            CR: 1.02 (0.79, 1.31);            PoA: 2.41 (1.09, 1.80)</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	Continued	Continued	Severe eczema: SPW: 2.58 (1.94, 3.44); SA: 0.92 (0.65, 1.30); CR: 0.71 (0.50, 1.02); PoA: NR (1.80, 3.22)
<b>Asia</b>			
<a href="#">Ho et al. (2007)</a> Taiwan Period of study: 1995–1996	Survey of 69,367 children ages 12–15 yr by questionnaire. The max likelihood estimation was carried out with Fisher’s scoring algorithm and GEE.	NR	SO <sub>2</sub> not significant in both sexes. However, SO <sub>2</sub> showed a reversal effect on monthly asthma attack rate. (Authors state that this reversal effect could be caused by the interaction of sulfur dioxide with the lowest 5% monthly temperature avg.)
<a href="#">Hwang et al. (2005)</a> Taiwan Period of study: 2001	A cross-sectional study consisting of 32,672 Taiwanese school children aged 6–15 yr old. Using a modified Chinese version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire collected information on each participant’s health, environmental exposures, and other variables. A two-stage hierarchical model consisting of logistic and linear regression analyses was used to account for variation among subjects in the first stage and variation among municipalities in the second stage.	2,000 (ppb): 3.53 (2.00)	Increased annual levels of NO <sub>x</sub> , CO, and O <sub>3</sub> were associated with an increased risk of childhood asthma levels. In both single- and copollutant models SO <sub>2</sub> was not found to be associated with the risk of asthma. Odds ratio (95% CI) (per 10 ppb SO <sub>2</sub> ) Single-pollutant model 0.874 (0.729, 1.054) Two-pollutant model NO <sub>x</sub> + SO <sub>2</sub> : 0.724 (0.545, 0.963) CO + SO <sub>2</sub> : 0.689 (0.542, 0.875) SO <sub>2</sub> + O <sub>3</sub> : 0.826 (0.674, 1.014)
<a href="#">Peters et al. (1996)</a> Hong Kong, China (Kwai Tsing and southern districts) Period of study: 1989–1991	Cohort of 3,521 children from two districts in Hong Kong with good and poor air quality prior to the 1990 legislation to reduce fuel sulfur levels. Analyses consisted of multivariate methods using logistic regression along with GEE to examine the effect of legislation implemented to	Annual avg (µg/m <sup>3</sup> ): Southern 1989: 11 1990: 8 1991: 7 Kwai Tsing 1989: 111 1990: 67 1991: 23	SO <sub>2</sub> emissions were reduced by 80% after institution of the legislation. The study does not provide effect estimates for individual pollutants.
Continued	reduce fuel sulfur levels on respiratory health.	Continued	Continued

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
<p><a href="#">Wang et al. (1999)</a> Kaohsiung City and Pintung, Taiwan</p> <p>Period of study: 1995–1996</p>	<p>A cross-sectional study consisting of 165,173 high school students aged 11–16 yr old residing in the communities of Kaohsiung City and Pintung in Taiwan from Oct 1995 to Jun 1996. Used a video and questionnaire developed by the International Study of Asthma and Allergies in Childhood (ISAAC). The association between air pollution and asthma was examined using logistic regression. In addition, the study performed a multiple logistic regression to examine the independent effects of risk factors of asthma after adjusting for age, sex, parents' education, and area of residence. The multiple logistic regression included pollutant concentrations to examine the combined effect.</p>	<p>Median: 1996 (ppm): 0.013</p>	<p>In the univariate analysis, increasing concentrations of TSP, SO<sub>2</sub>, NO<sub>2</sub>, CO, O<sub>3</sub>, and airborne dust were all found to be significantly associated with asthma. These univariate estimates are associated with concentrations above a cutoff (i.e., the median concentrations of each pollutant). In the multivariate analysis increasing concentrations of TSP, NO<sub>2</sub>, CO, O<sub>3</sub>, and airborne dust were significantly associated with asthma.</p> <p>Odds ratio (95% CI) (per 0.013 ppm SO<sub>2</sub>):</p> <p>Univariate analysis <math>\geq</math> 0.013 ppm: 1.05 (1.02, 1.09)</p> <p>Adjusted odds ratio (95% CI)</p> <p>Multivariate analysis 0.98 (0.95, 1.02)</p>
<b>Middle East</b>			
<p><a href="#">Dubnov et al. (2007)</a> Hadera and Pardes-Hanna, Israel</p> <p>Period of study: 1996 and 1999</p>	<p>Cohort of 1,492 school children (7–14 yr old) living near a major coal-fired power station. Subjects underwent pulmonary function tests (PFT) for forced vital capacity (FVC) and forced expiratory volume during the first second (FEV<sub>1</sub>) to examine the association between pulmonary function and long-term exposure to air pollution. Using stepwise multiple regression (SMR) and ordinary least squares regression (OLS) examined the multiplicative effect of NO<sub>x</sub> and SO<sub>2</sub> on pulmonary function.</p>	<p>1996 and 1999 avg (SD) (ppm): 12.9 (11.3)</p>	<p>Using an integrated concentration value (ICV), which equals the product of NO<sub>x</sub> concentration and SO<sub>2</sub> concentration when both concentrations individually exceed the half-hour reference level, found significant associations between exposure to air pollution and decrements in pulmonary function.</p> <p>All children: NO<sub>x</sub> × SO<sub>2</sub> ΔFVC (%) B = -0.004, <i>p</i> &lt; 0.001 ΔFEV<sub>1</sub> (%) B = -0.004, <i>p</i> &lt; 0.001</p> <p>Children in zone of highest concentration of air pollution:</p>

**Table 5S-4 (Continued): Summary of epidemiologic studies of long-term exposure to SO<sub>2</sub> and respiratory morbidity.**

Study	Methods	Pollutant Data	Findings
Continued	Continued	Continued	NO <sub>x</sub> × SO <sub>2</sub> ΔFVC (%) B = -0.005, <i>p</i> < 0.001 ΔFEV <sub>1</sub> (%) B = -0.005, <i>p</i> < 0.001
<b>Africa</b>			
<a href="#">Houssaini et al. (2007)</a> Morocco	Cross-sectional study of 1,318 children with a mean age of 12 yr. Used a questionnaire and medical diagnosis/reporting for asthma, and evaluated using Student's t-test, $\chi^2$ , odds ratios, and Cochran-Armitage tests.	Annual avg: 2000–2001: 60.2 µg/m <sup>3</sup> 2001–2002: 50.2 µg/m <sup>3</sup> 2002–2003: 49.6 µg/m <sup>3</sup> 2003–2004: 36.8 µg/m <sup>3</sup>	Significant prevalence for respiratory diseases, asthma, and infectious disease, when combined with TSP.

SO<sub>2</sub> = sulfur dioxide; TN = Tennessee; WI = Wisconsin; MO = Missouri; OH = Ohio; KS = Kansas; MA = Massachusetts; yr = year; h = hour; mo = month; CI = confidence interval; U.S. = United States of America; ppb = parts per billion; TSP = total suspended solids; COPD = chronic obstructive pulmonary disease; g = gram; m = meter; O<sub>3</sub> = ozone; NO<sub>2</sub> = nitrogen dioxide; CO = carbon monoxide; PM = particulate matter; SD = standard deviation; IQR = interquartile range; *p* = probability; FVC = forced vital capacity; FEV = forced expiratory volume; SAPALDIA = Swiss Study on Air Pollution and Lung Disease in Adults; SCARPOL = Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution; SES = socioeconomic status; GEE = generalized estimating equations; km = kilometer; avg = average; PEF = peak expiratory flow; GSHPx = glutathione peroxidase; SOD = superoxide dismutase; MDA = catalase malondialdehyde; FEF = forced expiratory flow; ETS = environmental tobacco smoke; KIGA = Study on Airway Diseases and Allergies among Kindergarten Children; LISS = Leipzig Infection, Airway Disease, and Allergy Study on School Starters; dpd = difference per day; PMSEAD = Polish Multicentre Study of Epidemiology of Allergic Diseases; BS = black smoke; AR = airway responsiveness; EIB = exercise-induced bronchial reactivity; SAVIAH = Small-Area Variation in Air Pollution and Health; BHR = bronchial hyperresponsiveness; SPW = São Paulo West; SPS = São Paulo South; PoA = Porto Alegre; CR = Curitiba; SA = Santo André; PFT = pulmonary function tests; SMR = stepwise multiple regression; OLS = ordinary least squares regression; ICV = integrated concentration value; ASHMOG = Adventist Health Air Pollution Study; NCI – National Cancer Institute; NHANES = National Health and Nutrition Examination Survey; MEF<sub>50</sub> = maximal expiratory flow at 50%; RR = relative risk; ISAAC = International Study of Asthma and Allergies in Children; LISS = Leipzig Infection, Airway Disease, and Allergy Study on School Starters.