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Annual SO₂ exposure, asthma, atopy, and lung function in Puerto Rican children

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Abstract

Background: Long-term effects of sulfur dioxide (SO₂) exposure on children, a vulnerable population, are largely unknown. Further, how long-term SO₂ affects Puerto Rican children living in the island of Puerto Rico, a group with high asthma prevalence, is unclear. We evaluated the effects of annual average 1-hr daily maximum SO₂ average on asthma, atopy, total IgE, and lung function in Puerto Rican children.

Methods: A cohort of 678 children (351 with asthma, 327 without asthma) was recruited in Puerto Rico from 2009–2010. Annual average 1-hr daily maximum SO₂ exposure was interpolated utilizing publicly available monitoring data. Multivariable logistic and linear regression was used for the analysis of asthma, atopy (defined as an IgE ≥ 0.35 IU/mL to at least one of five common aero-allergens), total IgE, and lung function measures (FVC, FEV1, and FEV1/FVC ratio).

Results: Annual SO₂ exposure [per 1 ppb] was significantly associated with asthma (odds ratio [OR]=1.42, 95% confidence interval [CI]=1.05 to 1.91) and atopy (OR=1.35, 95% CI=1.02 to 1.78). Such exposure was also significantly associated with lower FEV1/FVC in all children (β= -1.42, 95% CI= -2.78 to -0.08) and in children with asthma (β= -2.39, 95% CI= -4.31 to -0.46). Annual SO₂ exposure was not significantly associated with total IgE, FEV1, or FVC.

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Conclusions: Among Puerto Rican children in Puerto Rico, long-term SO₂ exposure is linked to asthma and atopy. In these children, long-term SO₂ exposure is also associated with reduced FEV1/FVC, particularly in those with asthma.

Keywords

SO₂ exposure; asthma; atopy; air pollution; Puerto Rican children; lung function

INTRODUCTION

Compared with adults, children are more susceptible to the detrimental effects of air pollution on respiratory health because of increased mouth breathing and ventilation per body weight, time spent outdoors, and an immature and still developing respiratory system^{1,2}. Indeed, the Children's Health Study demonstrated reduced lung growth in children exposed to poor air quality,^{3,4} and further showed that lung growth improved with air quality improvement⁵.

Sulfur dioxide (SO₂) is a pollutant predominantly emitted from fossil fuel combustion. Although short-term exposure to SO₂ leads to respiratory symptoms in children with asthma, less is known about the long-term effects of chronic SO₂ exposure on asthma, allergic sensitization (atopy) or lung function in children⁶⁻⁸.

In the United States (U.S.), Puerto Rican children are disproportionately affected with asthma⁹. Among Puerto Rican children, those living in the island of Puerto Rico have even greater morbidity from asthma than those living in the U.S. mainland¹⁰, perhaps due to insufficiently characterized variability in environmental factors and healthcare access.

In a previous study of children in Puerto Rico, we showed that living near a major highway (a broad marker of exposure to traffic-related air pollution) is associated with severe asthma exacerbations¹¹. Moreover, a prior study found early life SO₂ exposure was associated with an asthma diagnosis in children living in Puerto Rico, though such association became non-significant in a multi-site analysis. Further, that study was limited by the availability of only 2 air pollution monitors in the island of Puerto Rico¹².

On the basis of prior findings from our group and others, we hypothesized that chronic SO₂ exposure is associated with asthma, atopy, and decreased lung function among children in Puerto Rico. We tested this hypothesis in a case-control study of Puerto Rican children living in the metropolitan area of San Juan and Caguas (Puerto Rico).

METHODS

Study Population

Subject recruitment and study procedures have been described in detail elsewhere¹³. In brief, from March 2009 to June 2010 children ages 6–14 years residing in the metropolitan area of San Juan and Caguas (Puerto Rico) were selected from randomly selected households using a multistage probability sample design. Primary sampling units were randomly selected neighborhood clusters based on the 2000 U.S. census, and secondary sampling units were

randomly selected households within each individual primary sampling unit. A total of 6,401 households selected for inclusion were contacted. Of these, 1,111 households had 1 child who met inclusion criteria other than age (having four Puerto Rican grandparents). Of these 1,111 households, 438 (39.4%) had 1 eligible child with asthma (defined as having physician-diagnosed asthma and at least one episode of wheeze in the prior year). From these 438 households, one child with asthma was selected (at random if there was more than one such child). Similarly, only one child without asthma (no prior diagnosis of asthma and no wheeze in the previous year) was randomly selected from the remaining 673 households. In order to reach our target sample size (~700 children), we attempted to enroll 783 of the 1,111 eligible children. Parents of 105 (13.4%) of these 783 children refused to participate or could not be reached, leaving 678 study participants (351 cases and 327 control subjects). There were no significant differences in age, gender, or area of residence between children who did (n=678) and did not (n=105) agree to participate (E-Table 1).

SO₂ exposure assessment

The home address of each study participant was geocoded to a 15-digit 2000 U.S. Census Federal Information Processing Standard (FIPS) + block code at the University of Puerto Rico. Using the program ArcMAP10.1 (ArcGIS 10.1, Esri, Redlands, CA), centroids were created by obtaining X, Y coordinates for the center of individual census blocks based on a 2000 US Census map for Puerto Rico. One participant was removed from this analysis because of an unconfirmed address. The daily SO₂ 1-hour max [ppb] was downloaded from the Environmental Protection Agency (EPA) website for all SO₂ monitors on the island of Puerto Rico during 2008–2010. Utilizing ArcMAP 10.5 (ArcGIS 10.5, Esri, Redlands CA), the daily 1-hour maximum SO₂ average in the twelve months prior to enrollment was interpolated for each participant centroid via inverse distance-squared weighting for monitors within 50 km, as in prior studies^{12,14}. On the basis of the distribution of participant centroids and SO₂ monitors, a maximum of 10 monitors were used (E-Figure 1). We limited SO₂ exposure assessment to the year prior to enrollment, as we did not have complete residential histories for previous years. To reduce exposure misclassification, study participants who reported living at their current address for less than 1 year (n=37) or duration was missing (n=2) were excluded from this analysis¹⁵. In sensitivity analyses, SO₂ was additionally interpolated (estimated) for each centroid as the: (1) yearly average of the 4 monitors located within the 7 counties of the study for each month/year of enrollment, and (2) average annual SO₂ for month/year of enrollment for the nearest monitor. For further sensitivity analysis, our primary exposure (SO₂ interpolated by inverse-distance squared weighting) was limited to data from monitors with 75% of observations (defined as number of daily observations divided by 365 days), and with 50% of observations.

Study Procedures

Study participants completed a protocol that included administration of questionnaires, spirometry, and collection of blood samples. The child's parents completed a questionnaire that was slightly modified from one used in the Collaborative Study of the Genetics of Asthma¹⁶. This questionnaire was used to obtain information about the child's general and respiratory health, socio-demographic characteristics, family history, current second-hand

tobacco smoke (SHS) exposure, and use of inhaled corticosteroids (ICS) in the previous 6 months. Proximity to a major roadway was measured as previously described¹¹.

Spirometry was conducted with an EasyOne spirometer (NDD Medical Technologies, Andover, MA). All subjects had to be free of respiratory illnesses for 4 weeks before spirometry, and they were also instructed (when possible) to avoid use of inhaled short- and long-acting bronchodilators for 4 and 12 hours before testing, respectively. Forced expiratory maneuvers were judged to be acceptable if they met or exceeded American Thoracic Society criteria modified for children¹⁷. The best forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) were selected for data analysis. Percent predicted values were obtained utilizing the Global Lung Initiative (GLI) 2012 prediction equations¹⁸.

Serum levels of total immunoglobulin E (IgE) and IgE to each of five common allergens in Puerto Rico (house dust mite [Der p 1], cockroach [Bla g 2], cat dander [Fel d 1], dog dander [Can f 1], and mouse urinary protein [Mus m 1]) were measured with the UniCAP 100 system (Pharmacia & Upjohn, Kalamazoo, Mich). For each allergen, an IgE level of 0.35 kU/L was considered positive.

Written parental consent was obtained for participating children, from whom written assent was also obtained. The study was approved by Institutional Review Boards of the University of Puerto Rico (San Juan, PR; Protocol # 0160507) and the University of Pittsburgh (Pittsburgh, PA; Protocol # PRO-10030498).

Statistical Analysis

Our exposure of interest was annual average 1-hr daily max SO₂ [ppb]. Our outcomes of interest were asthma (defined above), atopy (defined as a positive IgE to at least one of the allergens tested), total IgE (log-10 transformed), and lung function measures (forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), and FEV₁/FVC). Wilcoxon rank sum or χ^2 was used for comparison of variables between groups, as appropriate. Logistic regression was used for the multivariable analysis of SO₂ exposure and asthma or atopy, which was adjusted for age, sex, household income, SHS exposure, body mass index (BMI) z-score, and residential distance to a major highway (to account for overall traffic-related air pollution¹¹); models for asthma were additionally adjusted for parental history of asthma, and those for atopy were additionally adjusted for parental history of allergic rhinitis and asthma. Multivariable linear regression was used for the analysis of SO₂ and total IgE or lung function measures. The analysis of lung function measures (as percent predicted values) was first conducted in all participants and then separately in cases and control subjects. This analysis was adjusted for annual household income, SHS exposure, BMI z-score, distance to a major roadway, and (in all participants) asthma status. Puerto Rico, as an equatorial US territory, has a relatively fewer seasonal fluctuations. Because SO₂ exposure represented yearly averages, we did not adjust for temperature or season. For all outcomes (other than asthma status), we included an asthma*SO₂ exposure term to assess for interaction. An interaction term was considered for inclusion in the final models if significant at alpha <0.05.

RESULTS

Table 1 shows the main characteristics of study participants. Children with asthma (cases) had higher annual average 1-hr daily max SO₂ exposure than control subjects (median 3.84 ppb vs. 3.64 ppb, $P < 0.01$). This was consistent in all sensitivity analyses (E- Table 2). Among the 638 children living at their address for at least 1 year, the average residence length was 7 years and the average participant's age was 10 years. Compared with control subjects, cases were significantly more likely to be atopic and currently exposed to SHS, and to have: a parental history of asthma and allergic rhinitis, higher BMI and total IgE, and lower percent predicted values for FEV1 and FEV1/FVC. Of all 1-hr daily max SO₂ monitor observations available, the EPA 1-hr daily maximum SO₂ standard of 75 ppb was only exceeded on 6 days (E- Table 3). Most (98%) of the study participants were born in Puerto Rico.

Table 2 shows the results of the unadjusted and adjusted analyses of annual 1-hour daily maximum SO₂ exposure and asthma, atopy, and total IgE. In a multivariable analysis adjusting for parental history of asthma, atopy, and other covariates, SO₂ exposure was significantly associated with 1.43 times increased odds of asthma (Model 1). This finding was essentially unchanged after additional adjustment for residential distance to a major highway (Model 2).

After adjustment for parental history of allergic rhinitis and other covariates, SO₂ exposure was significantly associated with 1.35 times increased odds of atopy (Model 1), but the magnitude and significance of this association were attenuated after adjustment for asthma and residential distance to a major highway (Model 2). Different interpolation methods yielded similar results (E- Tables 4 & 5), but the magnitude and precision of the effect estimate for asthma was reduced for the approach assessing SO₂ exposure by nearest monitor. All interpolation methods demonstrated an association between SO₂ exposure and atopy in both unadjusted and adjusted analyses. Likewise, all interpolation methods demonstrated an association between SO₂ exposure and total IgE, though such associations were not statistically significant at $P < 0.05$ after adjustment for covariates.

The results of the analysis of SO₂ exposure and percent predicted lung function measures is shown in Table 3. In a multivariable analysis, each ppb increment in SO₂ exposure was significantly associated with 1.42% lower percent predicted FEV1/FVC. In this analysis, SO₂ exposure was not significantly associated with percent predicted FEV1 or FVC, although asthma status (case vs. control) was associated with reduced FVC and FEV1. Given known effects of asthma on lung function, we then conducted an analysis stratified by asthma status (Table 4). In this stratified analysis, each ppb increment in SO₂ exposure was significantly associated with lower (by 2.39) percent predicted FEV1/FVC in children with asthma, but not in control subjects. SO₂ exposure was not significantly associated with percent predicted FEV1 or FVC in cases or in control subjects. Interpolation methods yielded similar results for FEV1/FVC, although again the magnitude and significance of the effect estimates were reduced for the approach assessing SO₂ exposure by the nearest monitor (E- Tables 6 & 7).

A sensitivity analysis for missing data yielded results consistent with those of our primary analysis (E-Tables 8–12). None of the interaction terms (SO_2 *asthma) were significant for any outcome. Moreover, no interaction term was significant in any sensitivity analyses for any outcome, with one exception: FEV1/FVC ratio & SO_2 as average of the four monitors in the study area ($P=0.03$, E-Table 6). However, such interaction became non-statistically significant after correction for multiple testing.

DISCUSSION

We found that long-term annual average 1-hr daily max SO_2 exposure is associated with asthma and atopy in Puerto Rican children living in the island of Puerto Rico. Moreover, SO_2 exposure is associated with reduced FEV1/FVC in children with asthma. Such findings are noteworthy for an area not exceeding current EPA standards for SO_2 levels.

SO_2 exposure has been associated with asthma in some^{12,14} but not all^{12,15,19,20} previous studies. Compared with assessment of short-term SO_2 exposure, measuring long-term SO_2 exposure is rarely feasible and thus different interpolation methodologies are employed. This, along with local and regional heterogeneity in air pollutants, pose comparative challenges. To improve comparability, we used an interpolation technique similar to previously described^{12,14}. Our findings are consistent with those from a prior study that reported an association between SO_2 exposure in the first year of life and asthma among children in the island of Puerto Rico (OR for each 1 ppb increment daily average= 1.10, 95% CI= 1.01–1.19)¹², as well as those from a study of medical records data that reported an association between SO_2 exposure *in utero* and in the first year of life and asthma among Canadian children and adults younger than 35 years (OR for every 1 $\mu\text{g}/\text{m}^3$ increase =1.03, 95% CI=1.02–1.05)¹⁴. The estimated annual 24-hour average of SO_2 in the previous study in Puerto Rico (4.1ppb, SE=2.0 for 1996) was similar to that in our current study of 1-hour daily max SO_2 average (mean 3.9 ppb, SE=0.7, 2008–2010). The SO_2 primary national ambient air quality standard changed in 2010, adding complexity to annual SO_2 comparisons (revoked 24-hour and annual standard and replaced with 1-hr max), though the reduced SO_2 between studies mirrors the overall U.S. trend of reduced SO_2 ²¹. Of interest, however, SO_2 exposure in the first year of life was not significantly associated with asthma in a combined analysis of all children participating in that prior study, which included not only children in Puerto Rico but also children in the U.S. mainland¹². Thus, regional air pollution composition and interactions with region-specific environmental exposures may modify the effects of SO_2 exposure on asthma.

EPA Air Quality System air monitoring data does not allow for identification of the source(s) of SO_2 . The largest source of SO_2 is from fossil fuel combustion used in energy generation (e.g., power plants) and industrial facilities, and to a lesser extent from transportation burning high-sulfur content fuels (e.g. shipping)²². Until 2012, two thirds of the energy production in Puerto Rico was from petroleum, with the remaining third from natural gas and coal²³. Puerto Rico's energy consumption is a third of the 50 states' per capita consumption, yet petroleum consumption is 75% of the average for those states, due to dependence on residential fuel oil and diesel fuel for electricity²³.

Consistent with our results for atopy in Puerto Rican children, SO₂ has been associated with allergic sensitization in guinea pigs²⁴ and lifetime allergic rhinitis in children²⁵. In contrast to our findings, some ecological studies showed no difference in the prevalence of hay fever or allergy between residents of West German cities (less polluted) and those of East German cities (more industrial, with increased SO₂ levels)⁸. Although SO₂ exposure was associated with increased total IgE, such association did not reach statistical significance at P<0.05. This could be due to lack of statistical power due to sample size or a true negative association (as previously reported in adults)²⁶.

The mechanisms underlying the link between long-term SO₂ and asthma and atopy are unknown. A study of healthy mice reported that SO₂ exposure increased lung reactive oxygen species (ROS) and STAT6 mRNA expression (a regulator of Th2 responses²⁷). In ova-albumin sensitized mice, SO₂ exposure increased alveolar eosinophils and neutrophils, mucus hypersecretion, and Th2 cytokines (interleukin (IL)-4, IL-5, and IL-13)²⁸. These and other findings suggest that SO₂ induces airway oxidative stresses and promotes a Th2 (allergic) phenotype^{6,29,30}. In a separate study of SO₂ exposure and maple tree pollen, SO₂-exposed pollen (as compared to unexposed pollen) elicited increased IgE reactivity in human sera sensitized to the pollen, suggesting potentially increased allergenicity of co-exposure to maple pollen and SO₂³¹. This is consistent with findings for other air pollutants such as diesel exhaust particles (DEP), which has been shown to lead to increased ROS generation and proinflammatory states³². Similar to our results, DEP was not demonstrated to increase total IgE but has been shown to promote allergic sensitization including neo-sensitization^{33,34}. Other epidemiological studies have demonstrated an association between air pollutants other than SO₂ (e.g. particulate matter (PM), nitrogen dioxide (NO₂)) and atopy.

Current evidence supports a strong link between short-term SO₂ exposure and reduced lung function in persons with asthma^{30,35}. On the other hand, there is inconsistent evidence of an association between long-term SO₂ exposure and lung function, likely due to varying methodologies, with some studies reporting deficits^{36,37} and others reporting no changes^{38–40} in lung function. Many studies have reported an inverse association between SO₂ exposure and FVC or FEV₁, but not with FEV₁/FVC. However, results from some prior studies are consistent with our finding of no association between SO₂ exposure and FVC or FEV₁^{38,40}.

Our finding of an inverse association between SO₂ exposure and FEV₁/FVC in children with asthma contrast with those from a prior negative study in children with mild-moderate asthma⁴⁰ but are generally consistent with those from a community-based study of children and adults (5–70 years old)³⁷. SO₂ has been shown to have potentially enhanced negative effects on lung function in persons with asthma who also have a TNF- α polymorphism at position -307 (wild type GG)⁴¹, and thus children with and without asthma may have varying susceptibilities to SO₂.

Children with asthma are more susceptible to the deleterious effects of air pollution⁴². Persons with asthma have been demonstrated to have increased susceptibility to SO₂ for

reasons that are incompletely understood⁶ but may include co-existing conditions such as obesity, chronic stress, and nutrient deficiencies⁴³.

We recognize several study limitations. First, personal SO₂ exposures were not measured and relatively simple interpolation methods were employed, which can lead to exposure misclassification. However, we would expect such misclassification to be non-differential and thus bias our results towards the null hypothesis. Second, SO₂ could be a proxy for unmeasured (confounding) pollutants. For example, SO₂ has been found to correlate with PM^{26,38}, with some studies reporting independent effects of SO₂ effects in multipollutant models but not all⁷. Nonetheless, adjustment for proximity to a major roadway did not change our results for asthma. Third, we cannot assess temporal relationships (e.g., whether SO₂ exposure preceded asthma development) in this cross-sectional study. Fourth, we had limited data on adherence to ICS, which has been shown to attenuate some of detrimental effects of air pollution on lung function and asthma control in some studies but not in others^{40,44,45}.

In summary, annual 1-hr daily max SO₂ exposure was significantly associated with asthma and atopy among Puerto Rican children living in the island of Puerto Rico. Moreover, such SO₂ exposure was also significantly associated with reduced FEV₁/FVC (a marker of airflow obstruction) in children with asthma. Our findings suggest that SO₂, even at levels below currently recommended EPA standards, may contribute to the burden of asthma in high-risk Puerto Rican children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Baseline characteristics of study participants, by asthma status

	ALL	Controls	Cases
N=	638	308	330
Annual 1-hr daily max SO ₂ , ppb	3.80 (0.88)	3.64 (0.57)	3.84 (0.92) **
Age, years	10.2 (2.7)	10.5 (2.7)	10.0 (2.6) *
Gender, female	302 (47%)	158 (51%)	144 (44%)
Lived at current residence, years	7.2 (4.0)	7.6 (4.0)	6.9 (3.9) *
FVC %predicted	103 (17)	105 (18)	102 (16)
FEV1, % predicted	95 (15)	98 (15)	93 (16) **
FEV1/FVC, % predicted	92 (10)	94 (10)	91 (10) **
Income >\$15,000, yes	225 (36%)	110 (37%)	115 (35%)
Distance to a major roadway, meters	220 (324)	287 (364)	210 (269)
Current SHS exposure, yes	252 (40%)	104 (34%)	148 (45%) **
IgE, geometric mean	214 (4.9)	151 (4.7)	300 (4.8) **
Atopy	331 (59%)	135 (50%)	196 (69%) **
BMI, z score	0.59 (1.1)	0.49 (1.1)	0.69 (1.2) *
Parental history of asthma, yes	317 (50%)	98 (32%)	219 (67%) **
Parental history of allergic rhinitis, yes	125 (20%)	45 (15%)	80 (24%) **
Prescribed inhaled corticosteroid in last 6 months, yes	-	-	107 (32%)

Results reported as mean (sd), median (IQR) for SO₂ and distance, or n (%). Atopy defined as at least one positive (0.35kU/L) specific-IgE to aeroallergen (cat, dog, dust mite, cockroach, mouse). Percent predicted calculated based on Global Lung Initiative (GLI2012) prediction equations. Analysis restricted to participants who reported living at least 1 year at current residence. P value obtained from Wilcoxon rank sum or Chi square between no asthma and asthma groups.

* p value<0.05,

** p value <0.01

Table 2-

Multivariable analysis of annual 1-hour daily max SO₂ [ppb] and selected outcomes in Puerto Rican children living in San Juan Metropolitan Area

Outcome= Asthma[¥]			
	Unadjusted OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)
N=	638	535	535
Annual average 1-hr daily max SO ₂ , ppb	1.65 (1.29, 2.10) **	1.43 (1.06, 1.92) *	1.42 (1.05, 1.91) *
History of parental asthma	-	4.62 (3.15, 6.79) **	4.62 (3.14, 6.79) **
Atopy	-	2.14 (1.45, 3.17) **	2.19 (1.48, 3.24) **
Distance to a major roadway, per 100m	-	-	0.96 (0.89, 1.02)
Outcome= Atopy^t			
	Unadjusted OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)
N=	557	534	534
Annual average 1-hr daily max SO ₂ , ppb	1.38 (1.07, 1.79) *	1.35 (1.02, 1.78) *	1.27 (0.96, 1.68) ¶
History of parental allergic rhinitis	-	1.51 (0.95, 2.39)	1.32 (0.82, 2.11)
Asthma	-	-	2.06 (1.42, 3.00) **
Distance to major roadway, per 100m	-	-	1.07 (1.00, 1.14) *
Outcome= IgE[¶]			
	Unadjusted β (95% CI)	Model 1 β (95% CI)	Model 2 β (95% CI)
N=	557	535	535
Annual average 1-hr daily max SO ₂ , ppb	0.13 (0.04, 0.21) **	0.08 (-0.01, 0.17) ¶	0.08 (-0.01, 0.17) ¶
Asthma	-	0.26 (0.14, 0.37) **	0.26 (0.14, 0.38) **
Distance to major roadway, per 100m	-	-	0.013 (-0.01, 0.03)

Adjusted for age, sex, annual income \$15,000/year, current second-hand tobacco smoke exposure, BMI z score.

[¥] Physician-diagnosed asthma and wheeze in prior year.

^t At least one positive IgE (>0.35kU/L) to Allergies tested.

[¶] IgE log10 transformed for analyses, results per 1 unit log10

¶ p value <0.10;

* p value <0.05;

** p value <0.01

Table 3:

Multivariable analysis of annual 1-hour max SO₂ and spirometry variables in Puerto Rican children living in San Juan Metropolitan Area (n=505).

	FVC % predicted	FEV1 % predicted	FEV1/FVC % predicted
Annual average 1-hr daily max SO ₂ , ppb	0.92 (-1.21, 3.04)	-0.52 (-2.55, 1.51)	-1.42 (-2.78, -0.08) *
Asthma, yes	-2.70 (-5.48, 0.08)	-5.63 (-8.29, -2.97) **	-3.17 (-4.94, -1.39) **

Results displayed as β (95% CI). %predicted based on GLI2012 prediction equations. Adjusted for annual income \$15,000/year, current second-hand tobacco smoke exposure, BMI z score, distance to a major roadway (m).

*
p value <0.05;

**
p value <0.01

Table 4:

Multivariable analysis of annual average of 1-hour daily max SO₂ and FEV1/FVC (% predicted) in Puerto Rican children living in San Juan Metropolitan Area, by asthma status

	Controls	Asthma	
		Model 1	Model 2
N	244	261	261
Annual average 1-hr daily max SO ₂ , ppb	-0.43 (-2.35, 1.49)	-2.39 (-4.31, -0.46) *	-2.33 (-4.25, -0.41) *
Prescribed inhaled corticosteroid in the last 6 months, yes	-	-	-2.14 (-4.92, 0.63)

Results displayed as β (95% CI). %predicted based on GLI2012 prediction equations. Adjusted for annual income \$15,000/year, current second-hand tobacco smoke exposure, BMI z score, distance to a major roadway (m).

*
p value <0.05