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ABSTRACT

BACKGROUND: Endotoxin exposure is associated with airway inflammation. Children spend 6-8 hours a day in school, yet the effect of school-specific endotoxin exposure on asthma morbidity is not well understood.

METHODS: In this longitudinal cohort study, 248 students with asthma from 38 inner-city schools underwent baseline phenotyping and follow-up. Clinical outcomes were evaluated throughout the academic school year and linked to classroom-specific dust and air endotoxin levels as well as home dust endotoxin levels. The primary outcome was maximum asthma symptom days per two week period.

RESULTS: Classrooms had higher settled dust endotoxin levels compared to homes (14.3 vs. 11.3 EU/mg, $p=0.02$). 22.0% of classrooms had airborne endotoxin levels exceeding recommended occupational exposure limits for adults. Classroom air endotoxin levels were independently associated with increased maximum symptom days in non-atopic, but not in atopic asthmatics (interaction p -value 0.03). Adjusting for home exposures, classroom endotoxin exposure was independently associated with a dose-dependent increase in asthma symptom days for non-atopics (adjusted IRR 1.16 [1.03 – 1.31, $p=0.02$]). In these subjects, maximum symptom days increased by 1.3 days for each 14 day period when comparing students in classrooms with the lowest endotoxin levels compared to average measured levels.

CONCLUSIONS: Inner-city children with asthma are exposed to high levels of airborne endotoxin at school, resulting in increased asthma symptoms in non-atopic children. Mitigation of school-related exposures may represent a strategy to decrease asthma morbidity in this population.

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INTRODUCTION

Asthma affects over 300 million adults and children worldwide.¹ Inner-city children share a disproportionately large burden of disease due to asthma, and experience more severe asthma symptoms.² While the reason for this is multi-factorial, home-specific exposures have been identified as important,³ with multi-center studies showing that a home environmental intervention to reduce environmental risk factors can reduce asthma morbidity.⁴ Most of these studies have focused on the role of pollutants and allergens in sensitized asthmatics.

Endotoxin in homes has been demonstrated to increase wheeze,⁵ increase both airflow obstruction and bronchial hyper-reactivity in human challenge studies,⁶ and can potentiate the airway response to allergens in asthmatics.⁷ Endotoxin has also been identified as an important exposure in many occupational settings.⁸ The school is likely an occupational model for children, given that nearly every child spends the majority of his or her day in school. However, hardly anything is known about the role of school-specific endotoxin exposure on asthma morbidity, after adjusting for exposure in the home.

In this study, we aimed to test the hypothesis that school endotoxin exposure is associated with increased asthma symptoms independent of home endotoxin exposure, and to test whether the effect of school endotoxin exposure differs between atopic and non-atopic children with asthma.

METHODS

Study population

The School Inner-city Asthma Study (SICAS) is a single-center prospective cohort study of children with persistent asthma attending inner-city elementary schools in a northeastern United States city from 2008-2013. Children with persistent asthma attending these schools were recruited based on established inclusion and exclusion criterion modelled from other urban studies⁹ and adapted for SICAS; 1) history of physician diagnosed asthma and either current symptoms defined as cough, wheezing, shortness of breath, or whistling in the chest in the past 12 months, daily controller medication use, or unscheduled medical visits for asthma in the past year 2) attendance in grades kindergarten through 6th grade at a school where permission for environmental sampling had been obtained. The exclusion criteria included any significant pulmonary disease other than asthma. Written informed consent was obtained from each participant's parent or legal guardian, and assent was obtained from each participant. The protocol was approved by the institutional review board (protocol number 07-11-0465) as well as the participating school system.

Study procedures

Study procedures were as previously described,¹⁰ and as depicted in **Figure 1**. Screening questionnaires were collected each spring in participating schools to identify eligible asthmatics. Eligible subjects were invited to participate in a baseline comprehensive clinical phenotyping evaluation during the summer, which included: detailed questionnaire, allergy skin testing (MultiTest device, Lincoln Diagnostics, Decatur, IL) or specific IgE (ImmunoCAP, Phadia AB, Uppsala, Sweden) if skin testing was contraindicated, spirometry according to American Thoracic Society guidelines (Koko, Ferraris Respiratory, Louisville, CO), and exhaled nitric oxide (Niox MINO, Aerocrine,

New Providence, NJ). Home and classroom exposure samples were subsequently collected throughout the academic year and linked to enrolled students and their longitudinally collected health outcomes.

Follow-up phone surveys were administered by study staff approximately 3, 6, 9, and 12 months after the initial visit.

School exposure assessment was performed in the fall and spring of the school year. Classroom settled dust was collected with an Oreck XL (model BB870-AD, Oreck, LLC, Nashville, Tennessee) vacuum fitted on the inlet hose with a dust collector filter (DACI lab, Johns Hopkins, Baltimore, MD) using a standardized protocol.⁹ One week classroom airborne dust samples was collected using charged particle samplers (Quadra, Sharper Image, California) based on a validated protocol.^{11,12} Collected dust was extracted in buffered saline and the endotoxin content was measured using the Limulus amoebocyte lysate assay (BioWhittaker Inc., Walkersville, MD).

Every school year, approximately 75 eligible students were recruited from 8-10 participating schools, with 351 students completing baseline clinical phenotypic screening evaluations from 38 schools over the course of the study. Of the 351 asthmatics who participated in the baseline screening clinical evaluation, 280 eligible students had complete information on all relevant study variables (allergy testing, home, school exposure) and were eligible for follow-up in this study. Of the 280 subjects eligible for follow-up visits, 32 had missing relevant health outcome data during the academic school year of interest, leaving 248 subjects in the final analysis (**Figure 2**).

Outcome measures

The primary outcome was maximum asthma symptom days as used in prior urban asthma studies.^{3,4,13} It is defined as the largest of the following variables in the 2 weeks prior to each follow-up survey; 1) daytime wheezing, chest tightness, or cough OR 2) days on which child had to slow down or discontinue play activities due to wheezing, chest tightness, or cough OR 3) nights with wheezing, chest tightness, or cough leading to disturbed sleep (see **Supplement**).

Sensitization definition

Atopy was defined as any positive skin prick test to 14 common aeroallergens (with positive defined as a wheal diameter at least 3 mm larger than saline control) on intracutaneous testing or a specific IgE level of 0.35 kU/L or greater.

Statistical Analysis

Outcomes were linked to the temporally closest measured endotoxin level during the academic school year. Endotoxin levels were log transformed to minimize the impact of extreme values. All models included both classroom airborne and settled dust endotoxin as well as home settled dust endotoxin exposure. Age, gender, race, allergic sensitization, use of asthma controller medications, income (modeled as above vs. below \$25,000 a year), school and home settled dust mouse allergen were included in the final statistical models. Additional covariates such as body mass index were tested and were not significantly associated with the outcome or did not confound the exposure-response relationship. In order to adjust for the known nonlinear variation in asthma symptoms due to season, a penalized spline term for time since school start was fit using a generalized additive mixed effects model.^{13,14} Subject- and school-specific random intercepts were

included to account for within-subject and within-school correlation. 54.8 % of classrooms had only 1 study participant; thus classroom-specific random intercepts were not included. For count outcomes, Poisson additive mixed effects models accounting for overdispersion were applied. Interaction terms between school endotoxin levels and atopy were used to determine whether the effect of exposure differed by atopic status.

Prior reports have suggested that the relationship between airborne endotoxin and asthma symptoms may have an inverted U shape,¹⁵ with both very low and very high endotoxin levels associated with fewer asthma symptoms. Thus school air endotoxin was also modeled using a penalized spline term on non-log-transformed airborne endotoxin levels.

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All statistical analyses were performed in R 3.1.0. Generalized additive mixed effects models were fit using the gamm4 package.¹⁷ A two sided p-value <0.05 was considered statistically significant.

RESULTS

The children were on average 8 years old (range 4-13), and were predominantly Hispanic or African American (**Table 1**). Seventy percent lived in a single parent household, and 57.3% had an annual household income of \$25,000 or less. 69.5% were sensitized to at least one of the allergens tested, with the most common allergens being cat (37.4%), dust mite (33.3%), and mouse (30.1%). Half were on either an inhaled corticosteroid or a leukotriene modifier for asthma control. At the baseline screening visit, the average number of days with asthma symptoms in the prior two weeks was 2.7, although there was a seasonal rise in asthma symptoms peaking in the wintertime (**e-Figure 1**).

School dust endotoxin levels were significantly higher than home levels (14.3 vs. 11.2 EU/mg, $p=0.02$, **Table 2**). The average (geometric mean) school air endotoxin concentration was 24.7 EU/m³, whereas prior studies in urban Northeastern homes using a different sampling strategy report average air endotoxin levels of 0.8 EU/m³.¹⁸ 22.0% of classroom air endotoxin levels exceeded 90 EU/m³, a recommended occupational exposure limit for adults.¹⁹ Classroom air and dust endotoxin levels were not well correlated (Pearson correlation = 0.02, Spearman correlation = 0.14). There was significant variation of both air and settled dust endotoxin levels both within and between schools (**e-Figure 2**). After adjusting for school, there was no significant seasonal variation in either air or settled dust endotoxin levels.

In models simultaneously adjusting for school air, school dust, and home dust endotoxin levels, only school air endotoxin concentration was associated with asthma symptoms (**Table 3**). Although atopic asthmatics experience higher maximum symptom days than non-atopic asthmatics (IRR 1.86 [95% CI 1.09-3.17]), school air endotoxin levels increased asthma symptom days only in non-atopic asthmatics (adjusted IRR 1.16 [95% CI 1.03-1.31] for non-atopics, adjusted IRR 1.00 [95% CI 0.93-1.07] for atopics, atopy*school air endotoxin p -value 0.03).

When looking at the component outcomes that contribute to asthma symptoms, school air endotoxin exposure was associated with higher daytime wheeze and exercise-related symptoms, but was not associated with nighttime wheeze, in non-atopic asthmatics. Atopic asthmatics had significantly more nighttime wheeze than non-atopics overall, but school airborne endotoxin exposure was associated with decreased nighttime wheeze. For all symptom outcomes, the effect of school air endotoxin differed by atopy.

The effect of school air endotoxin exposure on maximum symptom days is depicted in **Figure 3**. On average, atopic asthmatics had higher maximum symptom days than non-atopic asthmatics. However, school air endotoxin exposure was associated with increased maximum symptom days only in non-atopic asthmatics. An increase in school air endotoxin from 0.2 EU/m³ (lowest measured classroom level) to 24.7 EU/m³ (average measured classroom level) was associated with a dose-dependent increase in maximum asthma symptom days of 1.3 days for each 14 day period.

To identify the functional form of the endotoxin exposure-response relationship, school air endotoxin was also modeled using a penalized spline term (**Figure 4**). In non-atopic subjects, higher concentrations of school air endotoxin was associated with increased maximum symptom days. In contrast, for atopics, there was an inverted U shaped relationship between school air endotoxin and maximum symptom days, where symptoms appeared to plateau at 230 EU/m³ then decrease at higher levels.

DISCUSSION

Through nearly a decade of community relationships, our study team has accomplished an unprecedented infrastructure, linking rigorous and extensive school/classroom and home specific environmental sampling with carefully phenotyped health effects in asthmatic children, allowing us to fully tease out school-specific environmental effects on health outcomes. Although we have previously identified higher settled dust school endotoxin levels compared to homes,²⁰ here we first report that airborne endotoxin levels are high in this inner-city setting, and in fact 22% of classrooms have airborne endotoxin levels exceeding recommended occupational limits for adults.¹⁹ In this longitudinal study,

we find that classroom-specific airborne endotoxin levels are independently associated with increased asthma symptoms in non-atopic children with asthma, after adjusting for home exposures. More important is the magnitude of effect, which has not previously been reported. Our study suggests that if classroom-specific airborne endotoxin levels are reduced from the average measured to the lowest measured levels, maximum asthma symptom days can be reduced by 1.4 days per two week period. This translates to 34 fewer days per year of symptoms for each affected child, which is comparable to the effect seen with inhaled corticosteroids in the Childhood Asthma Management Program,²¹ and is approximately three times the effect size as that previously described for the addition of omalizumab to guideline-based asthma therapy in inner-city children.¹³ High levels of school endotoxin exposure may explain why inner-city children experience a higher burden of disease and higher morbidity due to asthma, and represents an important potential area of intervention

In nearly all countries, school attendance is mandatory, and is in essence the occupation of children, who spend 6-8 hours daily in school. However, occupational limits of exposure currently do not apply to children in the school setting. Several non-US based studies have identified elevated airborne endotoxin levels in schools.^{22,23} A small fraction had levels exceeding recommended occupational exposure limits for adults;²² but overall levels in these non-inner city schools were lower than we report. A recent cross-sectional study based in the Netherlands did identify a trend towards an association between school endotoxin exposure and asthma-like symptoms in children without atopy;¹⁵ however, the association did not reach statistical significance. The investigators used passive air

samplers, making it difficult to compare results to most occupational studies, which use active air sampling techniques.

It is not surprising that high endotoxin exposure in the school setting increases symptoms in established asthmatics. In the laboratory setting, endotoxin induces potent host inflammatory responses, with increased airflow obstruction and bronchial hyper-reactivity lasting over 48 hours.⁶ What is more intriguing are the observed differences in the response of atopic vs. non-atopic asthmatics to school endotoxin exposure. This observation has been reported previously in a landmark study evaluating the effect of home endotoxin on asthma and allergy.²⁴ Opposing effects of endotoxin were seen in atopic vs non-atopic children, with a trend towards decreased wheeze in atopic children but a significant increase in wheeze in non-atopic children from non-farming households. Bronchial challenge studies in healthy subjects further demonstrate that atopy modifies the human response to endotoxin, with atopic subjects showing significantly decreased systemic inflammatory responses to inhaled endotoxin compared to non-atopic subjects.²⁵

It may seem puzzling that classroom-specific airborne endotoxin levels were associated with asthma morbidity whereas settled dust levels were not. The correlation between classroom-specific air and dust endotoxin levels was poor, consistent with other studies performed in the urban setting.¹⁸ Settled dust likely represents larger particles tracked in on the footwear of students, and are too large to become airborne and subsequently inhaled.

This study has several strengths. Repeated sampling in a school environment is extremely difficult to achieve given the need for environmental sampling procedures that do not

interfere with classroom activities. The study design was longitudinal as opposed to cross-sectional, allowing us to infer temporal associations. Although it is possible that endotoxin is a surrogate for other exposures such as pest infestation, we adjusted for mouse allergen exposure and found an independent effect of endotoxin on asthma morbidity. We also adjusted for potential unmeasured confounders exhibiting a seasonal variation such as rhinovirus infections, strengthening the validity of our findings.¹³

This study has some limitations. Home endotoxin exposure was limited to settled dust levels given feasibility. It is possible that home airborne endotoxin levels, if measured, is associated with differences in asthma morbidity. Air sampling was performed with an ion-charging device due to the need for unobtrusive air sampling during classes. We did not make any direct comparisons of our sampling techniques against other sampling methods, although this method has previously been shown to yield results comparable to pump-based sampling methods.^{11,12} Not all of the subjects who underwent a baseline screening evaluation in the summertime were eligible for participation in the study. There were no significant differences in baseline characteristics between those who had complete data and those who did not (**e-Table 1**), suggesting that a selection bias due to missing data was unlikely to have affected our conclusions.

CONCLUSIONS

In conclusion, we found that classroom-specific airborne endotoxin levels frequently exceeded recommended adult occupational limits. Higher school airborne endotoxin levels are associated with increased asthma symptoms in children with non-atopic asthma.

Mitigation of school-specific endotoxin exposures may be associated with decreased asthma morbidity in this population.

Contributors

PL and WP contributed to the conceptual design of this manuscript. WS, JG, and WP participated in the study implementation and data acquisition. WP established the cohort on which this study is based. PL participated in data analysis with input from CP and BC. PL, WS, JG, CP, BC, DG, WP participated in interpretation of the results. PL participated in the writing of the manuscript with input from all authors.

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FIGURE LEGENDS

Figure 1. Typical annual schema for subject recruitment, screening, enrollment, and study procedures. Fall was defined as the time period between September 1 to February 28, and spring as March 2 to the end of the academic school year.

Figure 2. Flow diagram of subject inclusion and exclusion.

Figure 3. Adjusted effect of school air endotoxin exposure on maximum symptom days, stratified by atopic status. Rug plot on bottom indicates values of school air endotoxin for which an observation was present. Increased school air endotoxin is associated with increased maximum symptom days in non-atopic asthmatics but not in atopic asthmatics. Note that atopic asthmatics have overall higher maximum symptom days, even though school air endotoxin is not associated with increased asthma symptom days in atopics.

Figure 4. Use of a penalized spline to determine the correct functional form of the relationship between school air endotoxin and maximum symptom days. Increased school air endotoxin levels is associated with increased maximum symptom days in non-atopic asthmatics. An inverted U shaped relationship exists between school air endotoxin and maximum symptom days for atopic asthmatics, where the lowest symptom days are seen at very low and very high endotoxin levels.

TABLES

Table 1. Baseline characteristics of the study population (n=248)

	n (%)
Demographic	
Age (y), median (range)	8 (4-13)
Male sex (%)	127 (52.6)
Race or ethnic group (%)	
Caucasian	11 (4.5)
African American	88 (35.8)
Hispanic	90 (36.6)
Mixed race	18 (7.3)
Other	39 (15.9)
Single parent household (%)	74 (69.9)
Annual household income < 25K (%)	142 (57.3)
Clinical	
<i>General</i>	
Family members with asthma (%)	198 (80.5)
Physician diagnosis of hay fever or allergic rhinitis (%)	29 (11.8)
Physician diagnosis of eczema (%)	113 (45.9)
<i>Healthcare and Medication Use</i>	
Hospitalization, past 12 months	18 (7.3%)
Unscheduled doctor's visit, past 12 months	93 (37.8)
Systemic steroids, past 12 months	24 (9.6)
Controller Medication Use ¹	137 (55.7)
Use of rescue inhaler $\geq$ 1/week	87 (35.3)
<i>Pulmonary Testing</i>	
FEV ₁ %, mean (SD) ²	102.7 (18.9)
FEV ₁ /FVC%, mean(SD) ²	99.0 (8.0)
FE _{NO} , parts per billion ³	
$\leq$ 25	62 (68.1)
26-44	20 (22.0)
$>$ 45	9 (9.9)
<i>Allergic Sensitization</i>	
$\geq$ 1 allergen	171 (69.5)
Cat	92 (37.4)
Cockroach	54 (22.0)
Dust mite	82 (33.3)
Dog	28 (11.4)
Mold	45 (18.3)
Mouse	74 (30.1)
<i>Symptoms</i>	
Maximum symptom days, mean (SD)	2.7 (4.0)

¹ Use of inhaled corticosteroid or leukotriene modifier as ascertained by review of active prescriptions during baseline screening visit.

² n=214, pre-bronchodilator. Both FEV₁ and FEV₁/FVC are reported as % predicted based on reference equations from the general US population.²⁶

³ n=91

Table 2. School and home endotoxin levels (248 homes, 188 classrooms, 38 schools)^a

Sampling Method	Location	Geometric Mean [range]	% Detectable
Air ^b	School	24.7 [0.2 – 780.0] EU/m ³	100%
Settled Dust ^c	School	14.3 [0.7 – 463.5] EU/mg	100%
Settled Dust	Home	11.3 [0.1 – 1697.7] EU/mg	97.6%

^a There were 187 fall and 188 spring airborne endotoxin measurements, 188 fall and 188 spring settled dust endotoxin measurements, obtained from 188 distinct classrooms in 38 schools. 248 fall settled dust measurements were obtained from 248 homes.

^b Home air sampling not performed. As a comparison, previous studies for urban Northeastern home report air endotoxin levels of 0.8 [0.01-30.2] EU/m³,¹⁸ although the air sampling strategy and laboratory where endotoxin analysis was performed differed from our study and may contribute to variability in measured levels.

^c School settled dust levels higher than home settled dust levels, p=0.02.

Table 3. Effect of school air endotoxin on asthma outcomes in atopic and non-atopic school age asthmatics. School and home settled dust endotoxin levels were not a significant predictor of asthma symptoms. Note that incidence risk ratios (IRR) depicted are for a 1 unit change in log transformed endotoxin units per cubic meter (log EU/m³). Numerically, this translates to an increase in maximum asthma symptom days of 1.3 days for each 14 day period when school air endotoxin levels increased from 0.2 EU/m³ (lowest measured classroom level) to 24.7 EU/m³ (average measured classroom level).

	Atopic		Non-atopic		Main effect	Interaction
	Crude IRR [95% CI]	Adjusted ^a IRR [95% CI]	Crude IRR [95% CI]	Adjusted ^a IRR [95% CI]	p-value ^{a,b}	p-value ^{a,b}
Maximum symptom days ^c	1.05 [0.99 - 1.12]	1.00 [0.93 - 1.08]	1.12 [1.02 - 1.23]	1.16 [1.03 - 1.31]	0.016	0.033
Daytime wheeze	1.06 [0.99 - 1.14]	1.04 [0.89 - 1.21]	1.10 [0.99 - 1.21]	1.21 [1.06 - 1.38]	0.005	0.046
Exercise-related symptoms	1.05 [0.96 - 1.16]	1.03 [0.92 - 1.14]	1.15 [1.01 - 1.31]	1.45 [1.19 - 1.77]	<0.001	0.003
Nighttime wheeze	0.94 [0.85 - 1.05]	0.83 [0.73 - 0.94]	1.13 [0.95 - 1.35]	1.07 [0.88 - 1.31]	0.501	0.030

Definition of abbreviations: CI = confidence interval; IRR = incidence rate ratio.

^aAdjusted for age, gender, race, annual income (above or below \$25,000), controller medication, home settled dust endotoxin, school settled dust endotoxin, home settled dust mouse allergen, school mouse settled dust allergen, and season.

^bAll models included the main effects of school airborne endotoxin concentration (log transformed) as well as the interaction term between atopy × school airborne endotoxin concentrations (log transformed).

^cMaximum number of days over prior 2 weeks with: 1) daytime wheezing, chest tightness, or cough OR 2) days on which child had to slow down or discontinue play activities due to wheezing, chest tightness, or cough OR 3) nights with wheezing, chest tightness, or cough leading to disturbed sleep

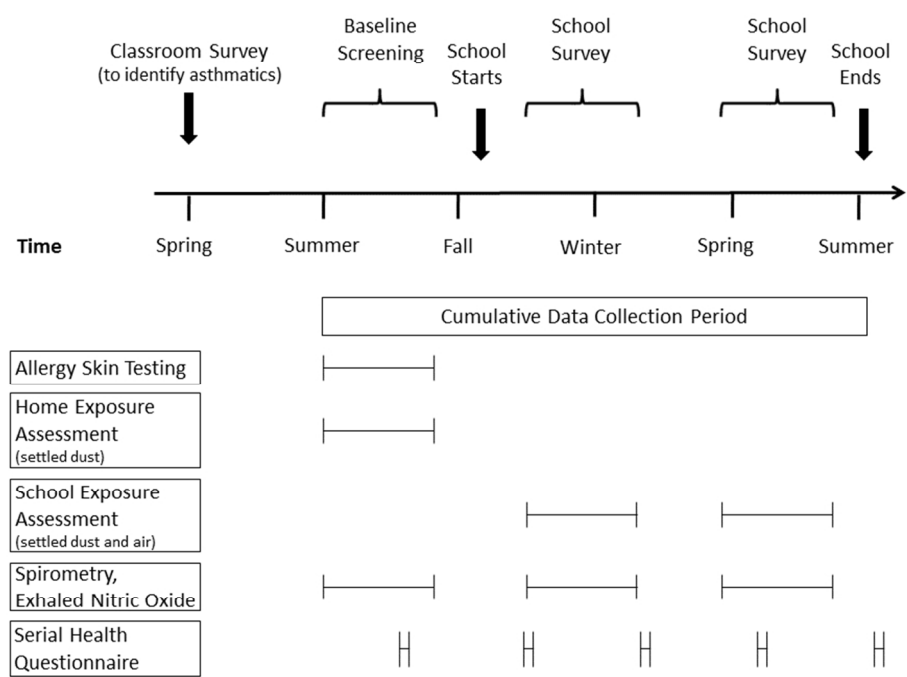


Figure 1. Typical annual schema for subject recruitment, screening, enrollment, and study procedures. Fall was defined as the time period between September 1 to February 28, and spring as March 2 to the end of the academic school year.

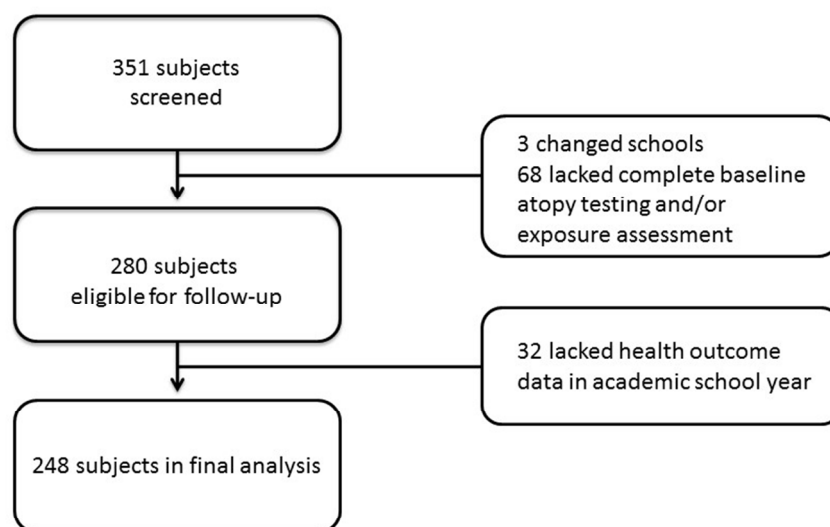
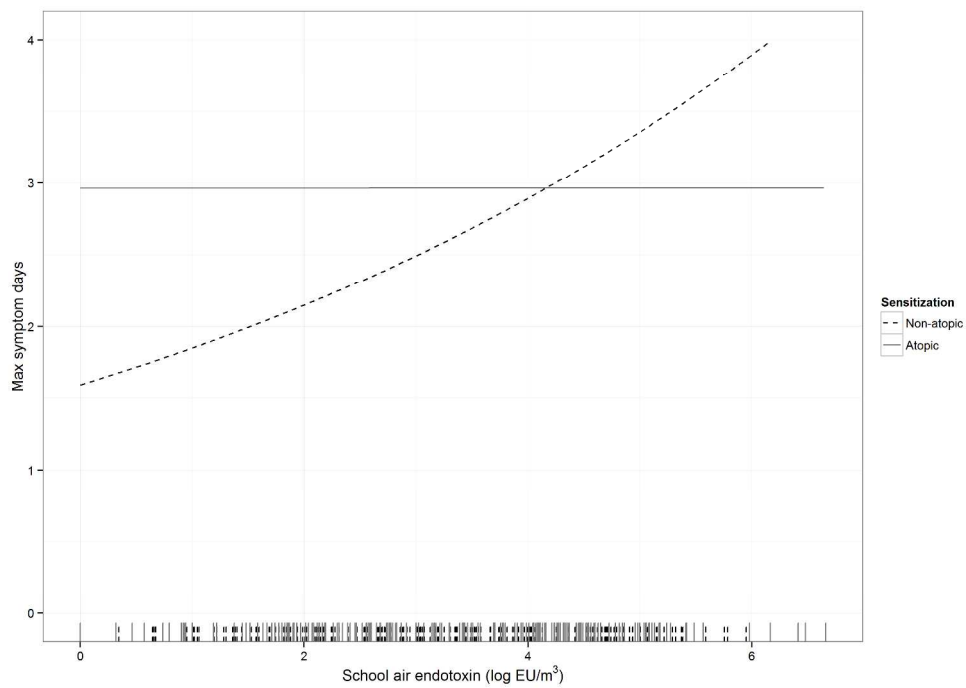
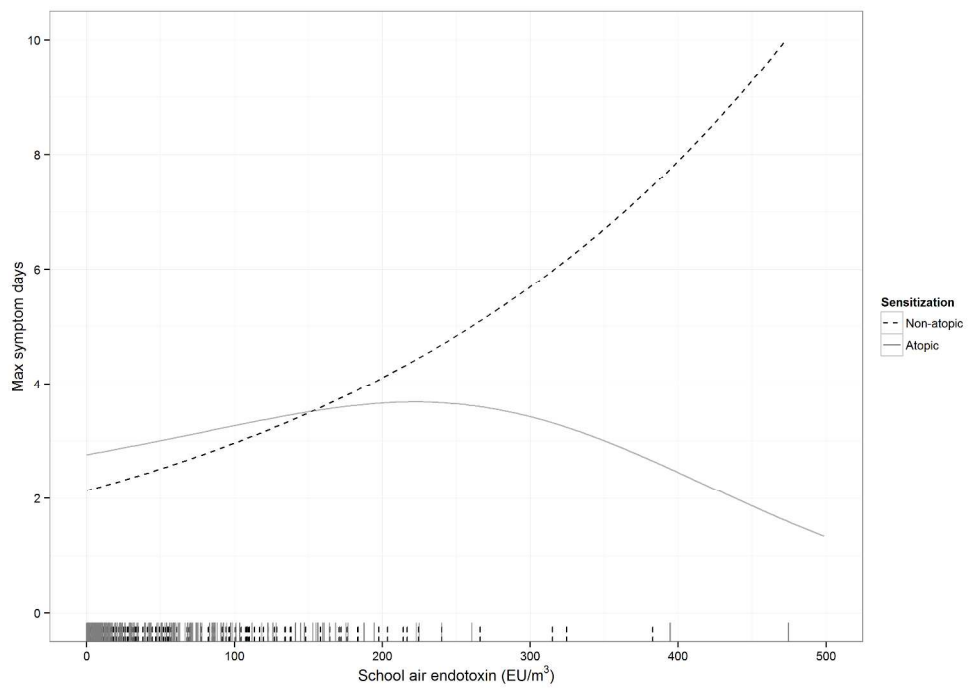


Figure 2. Flow diagram of subject inclusion and exclusion.
254x190mm (96 x 96 DPI)





ONLINE DATA SUPPLEMENT

SUPPLEMENTAL METHODS

Study procedures – Atopy

Allergy skin testing was used to define atopy. In the event that the participant took antihistamines, had eczema or hives on the day of testing that would interfere with skin prick testing, or preferred blood draw to skin prick testing, specific IgE was then used to define atopy instead of skin prick testing. Ultimately only 8 subjects received specific IgE testing to define atopy.

Primary outcome – maximum asthma symptom days

The maximum symptom day variable is based on standard questions used in all Inner City Asthma Consortium studies¹⁻³; this way of ascertaining asthma symptom days is validated, and allows comparability across studies. An interview with the subject's caregiver (in either English or Spanish based on respondent preference) was performed following a set script. The respondent was first prompted as follows: "Now I want to talk with you about how asthma affects [child's name] each day. The next few questions are about your child's health in the last two weeks, that is, in the past 14 days, from [14 days ago] to today."

The following questions were then asked to assess asthma symptom days:

- 1) "In the last 14 days, how many days did [child's name] have wheezing or tightness in the chest or cough?"
- 2) "In the last 14 days, how many days did [child's name] have to slow down or stop his/her play or activities because of asthma, wheezing or tightness in the chest, or cough?"
- 3) "In the last 14 nights, how many nights did [child's name] wake up because of asthma, wheezing or tightness in the chest, or cough?"

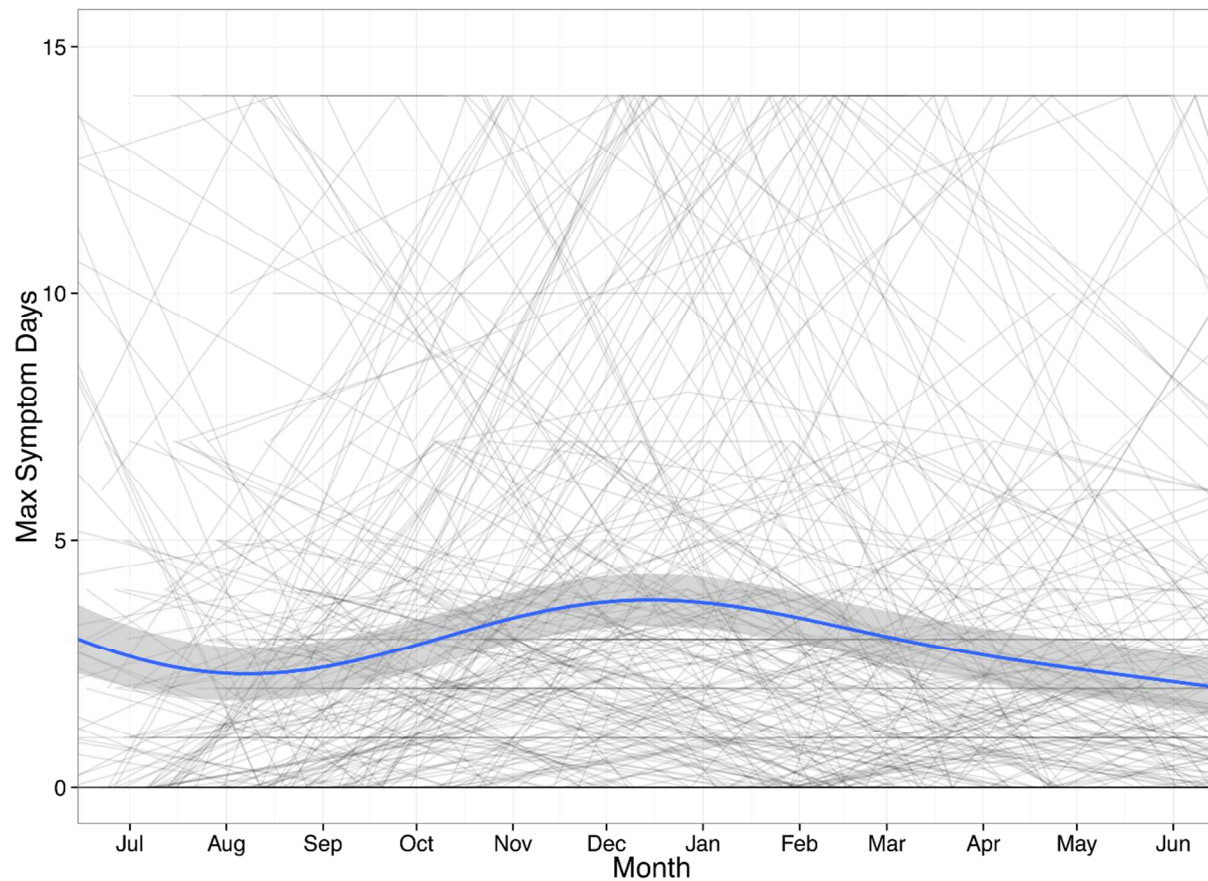
The script does not explicitly tell respondents to only respond based on symptoms distinct from a cold at the time of the interview.

SUPPLEMENTAL RESULTS

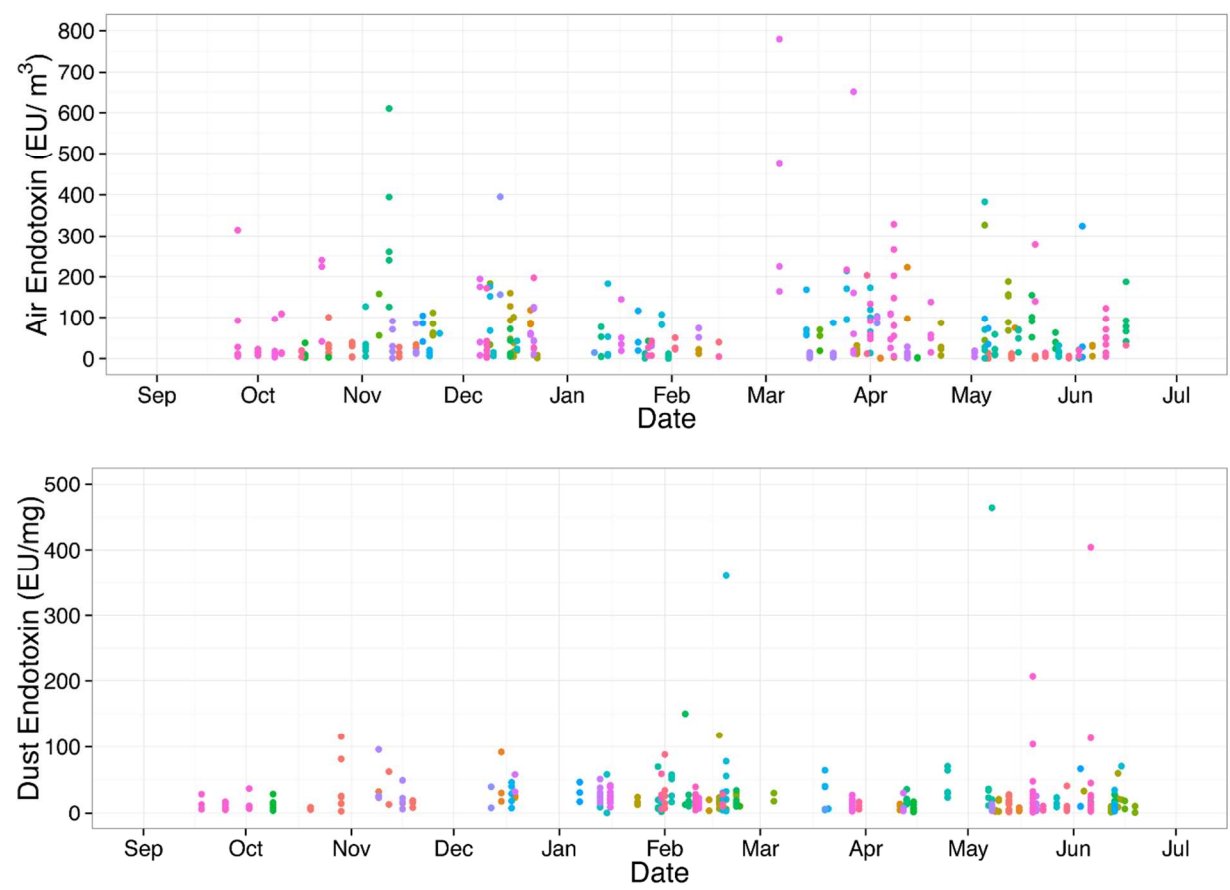
Effect modification by season A model incorporating a main effect of season (defined as fall vs. spring) as well as an interaction term between season and school air endotoxin levels (in addition to all other covariates used in the final outcome models) was fit. The interaction term was not significant (p-value = 0.93). Although we were not powered to examine effect modification by season, this result suggests that season is not an effect modifier of the relationship between school endotoxin exposure and asthma symptoms.

SUPPLEMENTAL FIGURES

e-Figure 1. Spaghetti plot where each line represents the trajectory of maximum symptom days for one individual over the academic school year. Blue line represents group average plotted using a penalized spline. Note the seasonal variation of maximum symptom days, with a peak in the winter and nadir in the summer.



e-Figure 2. School air and settled dust endotoxin levels over the academic school year. Each dot represents one classroom, and each school is represented by one color. Note significant variation both between and within schools.



SUPPLEMENTAL TABLES

e-Table 1. Baseline characteristics of the subjects not included in the final analysis (n=103)

	n (%)
Demographic	
Age (y), median (range)	8 (7-9)
Male sex (%)	57 (55.3)
Race or ethnic group (%)	
Caucasian	5(4.9)
African American	34 (33.0)
Hispanic	39 (37.9)
Mixed race	5 (4.9)
Other	20 (19.4)
Single parent household (%)	73 (70.9)
Annual household income < 25K (%)	64 (62.1)
Clinical	
<i>General</i>	
Family members with asthma (%)	83 (80.6)
Physician diagnosis of hay fever or allergic rhinitis (%)	16 (15.5)
Physician diagnosis of eczema (%)	49 (47.6)
<i>Healthcare and Medication Use</i>	
Hospitalization, past 12 months	7 (6.8%)
Unscheduled doctor's visit, past 12 months	47 (45.6)
Systemic steroids, past 12 months	10 (9.7)
Controller Medication Use ¹	59 (57.3)
Use of rescue inhaler >= 1/week	35 (34.0)
<i>Pulmonary Testing</i>	
FEV ₁ %, mean (SD) ²	98.3 (18.1)
FEV ₁ /FVC%, mean(SD) ²	96.9 (8.9)
FE _{NO} , parts per billion ³	
≤ 25	29 (76.3)
26-44	5 (13.2)
>45	4 (10.5)
<i>Allergic Sensitization</i> ⁴	
≥ 1 allergen	61 (59.2)
Cat	25 (24.3)
Cockroach	17 (16.5)
Dust mite	33 (32.0)
Dog	5 (4.9)
Mold	17 (16.5)
Mouse	21 (20.4)
<i>Symptoms</i>	
Maximum symptom days, mean (SD)	4.1 (4.8)

¹ Use of inhaled corticosteroid or leukotriene modifier² n=95, pre-bronchodilator³ n=38⁴ n=84, 19 subject did not have sensitization data

References cited

- 1 Rosenstreich DL, Eggleston P, Kattan M, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med* 1997; 336:1356-1363
- 2 Morgan WJ, Crain EF, Gruchalla RS, et al. Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med* 2004; 351:1068-1080
- 3 Busse WW, Morgan WJ, Gergen PJ, et al. Randomized trial of omalizumab (anti-IgE) for asthma in inner-city children. *N Engl J Med* 2011; 364:1005-1015